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IS THIAMIN THE ANTINEURITIC VITAMIN?*

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But here the paralysis is to be referred to some affection of the muscles, and not to the nerves. — James Jackson: On a peculiar disease resulting from the use of Ardent Spirits. *New Eng. J. Med. and Surg.* 9:351–353, 1822.

A SURVEY of the recent literature would seem to indicate that most authorities on nutrition and also some neurologists have now accepted the truth of the theory that the polyneuritis of beriberi, alcoholism and other nutritional disorders is caused by deficiency of thiamin. The following quotations from recent reviews serve to illustrate the general acceptance of this theory.

> The most constant and striking symptoms of a vitamin B_1 deficiency arise from degeneration in the nervous system. — Williams and Spies.[1]
>
> Beriberi . . . involves . . . a peripheral nerve atrophy (the so-called "polyneuritis"). It can be cured or prevented by vitamin B_1. — Harris.[2]
>
> We now feel that the vitamin B_1 deficiency theory of the genesis of so-called "alcoholic" polyneuritis is proved. — Jolliffe.[3]
>
> It is generally agreed that the peripheral neuritis of beriberi is caused by deficiency of this vitamin [B_1]. — Wilbur.[4]
>
> Clinicians have shown conclusively that peripheral neuritis may result from vitamin B_1 deficiency. — Wortis.[5]

If these statements are true, then polyneuritis of nutritional origin unassociated with evidence of other deficiencies requires no other treatment than the administration of pure synthetic thiamin. From the practical standpoint, this implication is obviously so important that it would seem worth while to reconsider carefully the evidence for the theory that thiamin deficiency is the cause of nutritional polyneuritis, before it passes on to be included among the accepted doctrines of medical science.

In this article an attempt is made to re-evaluate the evidence from the previous literature, and to offer some new interpretations which may serve to show that the present theory of the causation of nutritional polyneuritis rests on a far less secure foundation than currently expressed opinions would suggest.

EVIDENCE FROM LABORATORY INVESTIGATIONS

Ever since the earliest studies of the effects of vitamin B_1 deficiency in animals, the syndrome so produced has been considered as essentially similar to the human disease beriberi, just as blacktongue in dogs is considered the animal counterpart of human pellagra. Eijkman[6] was the first to show that a disease characterized by disorder of the nervous system could be produced in fowls by feeding them a diet of polished rice, which also constituted the staple food of Javanese prisoners suffering from beriberi. When some years later this work came to be repeated, it was clearly demonstrated, notably by Vedder and Clark,[7] that by suitable dietary means it was possible to produce in birds the anatomic changes of a true peripheral neuritis. These experiments were carried out before the differentiation of the vitamin B complex into more than one factor, and it is now certain in the light of present-day knowledge that the diets used were deficient not only in thiamin but also in the other components of the vitamin B complex. This peripheral neuritis, produced by a multiple deficiency, was rightly referred to as "polyneuritis gallinarum." Birds which developed this polyneuritis often showed evidence of marked disorder to the nervous system, characterized by the signs of inco-ordination and opisthotonos. For this reason the development of these signs came to be regarded as sufficient evidence for the presence of the anatomic lesions of polyneuritis. When, therefore, following the differentiation of vitamin

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B_1 from the remainder of the complex, it was subsequently shown that these signs also develop in animals deficient only in vitamin B_1, the condition produced by vitamin B_1 deficiency was referred to as polyneuritis, notwithstanding the fact that the presence of peripheral nerve changes was never clearly demonstrated in pure vitamin B_1 deficiency.

Today it is quite evident that the inco-ordination and opisthotonos which develop in animals suffering from thiamin deficiency are not the result of anatomic changes in peripheral nerves. In the first place, these signs have an acute onset, which is so rapid that they could hardly be due to the development of structural changes in the nervous system. Secondly, it is now known that the signs disappear within a few hours on the injection of thiamin, indicating that they are due to a disturbance of function rather than of structure. Furthermore, it has been shown that animals which develop these signs may show no anatomic changes in the peripheral nerves,[8-10] and that when such changes occur (perhaps as the result of some other associated deficiency), they are apparently not influenced by thiamin therapy.[9, 10] The work of Peters[11] and his school has clearly demonstrated that the nervous signs of thiamin deficiency in pigeons[12] and rats[13] are the result of a metabolic disorder (or "biochemical lesion") of the nervous tissue involving a defect in the process by which pyruvic acid is normally removed. Similar signs may be produced in pigeons by other factors disturbing normal metabolism, such as chloroform or insulin[14] and here there can be no question of any anatomic changes in the peripheral nerves.

It must be concluded that the signs by which thiamin deficiency in animals is ordinarily recognized are not the result of anatomic changes in the peripheral nerves, and that the fact that thiamin will cure these signs cannot be said to prove that thiamin is capable of curing polyneuritis in animals.

The foregoing argument must not be construed as implying that nutritional polyneuritis in animals is never the result of thiamin deficiency. Such a deduction would obviously be erroneous. Moreover, there is at least some theoretical evidence for thinking that thiamin deficiency might sometimes result in damage to peripheral nerves. It has been shown that thiamin is essential for the normal metabolism of nervous tissue, and although in acute deficiency few structural changes in the nerves are demonstrable, it is reasonable to suppose that the changes observed by Vedder and Clark,[7] and later by McCarrison[15] and by Kon and Drummond,[16] might result from prolonged though partial deficiency of thiamin. This, however, is difficult to prove experimentally, since thiamin deficiency results in anorexia and probably other disturbances of the gastrointestinal tract, which admit the possibility that defective assimilation and absorption of other factors contribute to the production of changes in the peripheral nerves.* That such other factors might well play a part is clearly indicated by the fact that anatomic changes in the peripheral nerves have been reported to occur in several other deficiency states in which the diet contained adequate amounts of thiamin. Mellanby[17] and Zimmerman and Cowgill[18] report demyelination of peripheral nerves in animals fed on a diet deficient in vitamin A. Zimmerman, Cowgill and Fox[19] also report peripheral neuritis in dogs fed on diets adequate in vitamin B_1 but lacking only the other factors in the vitamin B complex. Moreover, similar changes may occur in animals suffering from simple starvation.[20]

From the evidence accumulating from laboratory data the following conclusions may therefore be drawn.

Thiamin is capable of curing a specific metabolic disturbance of the nervous system in animals. This disturbance has been incorrectly referred to as "polyneuritis" by many authors, including myself.[21]

It is possible that chronic though partial deficiency of thiamin may result in true polyneuritis, but this does not appear to have been adequately demonstrated as yet.

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Thiamin deficiency in animals disturbs not only the normal metabolism of the nervous tissue, but also, and in a similar manner, the metabolism of the kidney, heart[22] and probably other organs. It so happens that the metabolic disturbance of the nervous tissue manifests it-

*Since this paper was submitted for publication, Swank (Swank, R. L.: Avian thiamin deficiency. *J. Exp. Med.* 71:683-702, 1940) has reported some careful histologic studies of the nervous system in thiamin deficiency. He has shown that in acute thiamin deficiency with opisthotonos the nerves may show few or no structural changes, but that in chronic thiamin deficiency, with leg weakness and sometimes evidence of cardiovascular beriberi, degenerative changes are present in both the peripheral nerves and the spinal cord. Furthermore, he has demonstrated that these degenerative changes may undergo repair following the administration of thiamin and, in most of his cases, normal mixed grain. However, I cannot agree that this establishes a direct causal relation between deficiency of thiamin and nerve degeneration. Apparently all the birds suffered from vomiting, which is evidence of impaired digestion, and introduces the probability that they were absorbing insufficient quantities of other factors besides thiamin. The improvement in digestion following treatment with thiamin might have an important influence in improving the absorption of other antineuritic factors, and this may well account for improvement in the histologic appearance of the nerves.

self externally in a dramatic manner, while a similar disorder proceeding in the kidneys and elsewhere produces no such obvious effects. This has given rise to the erroneous belief that thiamin has a specific effect on nervous tissue. It is probably safe to say that thiamin is necessary for the normal metabolism of almost all tissues. For this reason, and for the reasons summarized above, it would seem that so far as the evidence from laboratory experiments is concerned, there is really no great justification for referring to thiamin as the "antineuritic vitamin."

Application of Laboratory Knowledge to Clinical Problems

Since the earliest differentiation of the vitamin B complex into heat-labile (B_1) and heat-stable (B_2 or G) fractions, the former has been thought of as having two outstanding characteristics: first, that its deficiency in animals results in the signs of opisthotonos and inco-ordination (erroneously supposed to be evidence of anatomic polyneuritis); and secondly, that its deficiency in man results in the neurologic and cardiovascular manifestations of beriberi. In a similar manner vitamin B_2 was considered to be the heat-stable factor, deficiency of which resulted in loss of weight in rats and the development of pellagra in man. Subsequent laboratory work resulted in the chemical isolation of the heat-stable substance which prevents loss of weight in rats, namely, riboflavin. However, it was soon found that riboflavin was not effective in the cure of human pellagra. Likewise, the pure substance thiamin, which cures the nervous signs in animals, has now been isolated; but it does not necessarily follow that thiamin is capable of filling the role of the hypothetical "antiberiberi vitamin."

Following the successful synthesis of thiamin by Williams and Cline[23] in 1936, this substance for the first time became freely available for clinical trial. As a result, there is now evidence that the cardiovascular manifestations of beriberi may be cured by pure thiamin.[24] But evidence for the direct etiologic relation of thiamin deficiency to the neurologic manifestations of beriberi is less definite, and ought not to be accepted without critical consideration. Before proceeding to consider this evidence, mention should be made of some further relevant observations.

Student courses in elementary physiology have usually taught that beriberi is due to lack of antineuritic vitamin B_1, just as surely as scurvy is due to deficiency of vitamin C. Nevertheless, there is reason to believe that the clinical manifestations of beriberi may result from deficiency of more than one dietary factor. In the first place, it is worth remembering that human diets deficient in thiamin are almost inevitably deficient also in other components of the vitamin B complex. A diet consisting mainly of milled rice, such as is necessary to produce endemic beriberi in the Orient, can contain only small amounts of any of the factors in the vitamin B complex. Moreover, the neurologic and cardiovascular manifestations of beriberi as they occur in the Orient, and among alcoholic subjects in this country, are frequently associated with stomatitis,[25] dermatitis,[25] anemia[26] and spinal-cord changes[27] that are clearly not due to lack of thiamin. This is important in view of the evidence from animal experiments that nutritional polyneuritis may result from deficiency of dietary factors other than thiamin. On prima facie grounds, it would be rather surprising if it finally transpired that the two major manifestations of beriberi were in fact both due to thiamin deficiency, and that the associated deficiencies played only a minor part in the development of this syndrome. As stated by Wolbach,[10] "In all probability some of the features of this disease, as commonly seen, are due to other deficiencies."

Following the chemical identification of thiamin in 1936, the term vitamin B_1 has been generally regarded as synonymous with thiamin. Before that date, however, it was generally used by clinicians to mean no more than the hypothetical antiberiberi vitamin. For this reason, any writings prior to 1936 in which specific claims were made for the etiologic relation of vitamin B_1 deficiency to nutritional polyneuritis cannot with justification be quoted as expressions of the opinion that thiamin as now known was the factor concerned. Failure to appreciate this fact has led to several misinterpretations in recent literature.

Clinical Evidence

The Etiologic Identity of Alcoholic and Other Nutritional Neuritides with the Polyneuritis of Beriberi

Evidence has accumulated during the last ten years to show that in several conditions other than beriberi a nutritional polyneuritis may occur having essentially the same etiology as in the disease originally attributed to vitamin B_1 deficiency. The belief that lack of the antiberiberi vitamin may be the cause of polyneuritis occurring in a variety of diseases, including alcoholism, was first expressed by Shattuck[28] in 1928. Minot, Strauss and Cobb[29] were the first to study in detail a large group of cases of so-called "alcoholic" polyneuritis. They concluded that dietary deficiency played an important etiologic role in this

condition, and "probably especially lack of [anti-beriberi] vitamin B_1." Although pure thiamin was unavailable to these authors at the time, they are now quoted[30] as having shown that alcoholic polyneuritis is caused by lack of vitamin B_1 in the modern sense of the term, that is, of thiamin. Their observations and conclusions were supported by those of Meyer[31] and Wechsler.[32] Further evidence that alcoholic polyneuritis is primarily a nutritional deficiency was advanced by Strauss,[33] who showed that despite continued consumption of alcohol, patients with this disease showed clinical improvement when they received a nutritious diet together with various crude sources of the vitamin B complex. This was soon confirmed by the observations of Blankenhorn and Spies.[34] The opinions of all these authors are summed up in the statement by Strauss,[33] "Alcoholic polyneuritis may be regarded as similar to the polyneuritis of beriberi and treated accordingly," that is, by a high-vitamin, high-calorie diet, supplemented with yeast and liver extract to ensure a liberal supply of the hypothetical antineuritic factor. The efficacy of this treatment has lately been confirmed by Romano.[35]

In 1933, Strauss and McDonald[36] pointed out that polyneuritis of pregnancy responded well to similar treatment, and emphasized that this condition was essentially nutritional in origin and not due to toxins, as was then widely believed. They concluded: "Polyneuritis of pregnancy is probably a dietary deficiency disorder similar to beriberi. Rational therapy should aim to supply the deficiency, which may be especially some portion of the vitamin B complex." The same conclusion was reached by Fouts and his collaborators,[37] who emphasized the importance of the vitamin B complex in curing this condition. Nevertheless, recent authors[2, 5] have cited these two groups of workers as having successfully treated the polyneuritis of pregnancy with vitamin B_1 (thiamin).

In a later review, Strauss[38] pointed out that disorders of the gastrointestinal tract are liable to give rise to "conditioned" deficiency disease, including the peripheral neuritis characteristic of beriberi. This review has been cited[39] incorrectly as showing that the neuritis in these deficiencies has been relieved by thiamin.

Thus far, then, the work of the pre-thiamin era was concerned with establishing the clinical and etiologic identity of nutritional neuritis occurring in beriberi, alcoholism, pregnancy and gastrointestinal disturbances. The emphasis throughout was to the effect that adequate treatment of these conditions consisted in the administration of foods rich in the vitamin B complex. When in some cases a specific etiologic relation to vitamin B_1 deficiency was suggested, this implied no more than that these conditions were caused by deficiency of the hypothetical antineuritic vitamin, and it should not now be construed to mean that the authors believed nutritional polyneuritis to be due to deficiency of the pure chemical substance thiamin — a therapeutic agent entirely unavailable to them at the time.

The Relation Between Thiamin Deficiency and the Development of Polyneuritis

In 1935, Jolliffe and his collaborators[40] advanced evidence in favor of a close relation between nutritional polyneuritis and deficiency of vitamin B_1, in the sense of this term as then used by laboratory workers, that is, of thiamin. They accomplished the difficult task of obtaining from alcoholic addicts a sufficiently accurate dietary history to assess their consumption of thiamin and total caloric intake prior to admission. They used the formula,

$$\frac{\text{vitamin } B_1 \text{ (mg. equiv.)}}{\text{calories}} = 0.0000284 \times \text{body weight (gm.)},$$

which had been proposed by Cowgill on the basis of animal experiments in order to relate the thiamin requirements to caloric consumption and body weight. From this they concluded that polyneuritis occurred only in those subjects whose diet contained less thiamin than the amount called for by the estimated minimum requirement. However, this conclusion does not necessarily establish a causal relation between thiamin deficiency and polyneuritis. It should be remembered that diets deficient in one member of the vitamin B complex are almost certainly deficient in others. This is borne out by the observations of Elsom.[41] She also made use of Cowgill's formula in an experimental study on pregnant women in which the diets were carefully controlled, and showed that when the diet fell short of the estimated thiamin requirements macrocytic anemia developed, which indicated that the diet was then deficient in at least one other factor besides thiamin.

The Therapeutic Use of Thiamin in the Treatment of Polyneuritis

Sufficient time has elapsed since synthetic thiamin first became available for clinical use to give opportunity for an adequate clinical trial. A critical appraisal of the results so far reported therefore seems justified. The task of reviewing all the literature on the use of thiamin in the treatment of nervous disorders could not be accomplished in the space of a single article. No attempt will therefore be made to assess the value

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TABLE 1. *The Use of Thiamin in the Treatment of Polyneuritides.*

AUTHORS	DIAGNOSIS	No. OF CASES	DIET	THIAMIN THERAPY: DAILY DOSE	THIAMIN THERAPY: ROUTE	THIAMIN THERAPY: NO. OF DOSES	THIAMIN THERAPY: OTHER THERAPY	CRITERIA OF THERAPEUTIC RESPONSE: SENSORY: Hyperesthesia or Pain	SENSORY: Paresthesia	SENSORY: Hypoesthesia	SENSORY: Objective Sensory Changes	MOTOR: Inability to Walk	MOTOR: Weakness	MOTOR: Objective Motor Changes	No. OF CASES OF OTHER CONDITIONS REPORTED RELIEVED BY THIAMIN
				mg.											
Blankenhorn and Spies[26]	"Alcoholic" pellagra	1	Pellagra-producing	15	By mouth	15	Whisky	+				+			
Vorhaus, Williams and Waterman[43]	Neuritis, all types	92		10	By mouth			+	+				+		
Neumann[44]	Alcoholic polyneuritis	1		4	Subcutaneously	5		"Better"				+			Postdiphtheritic paralysis (1) Combined system disease (1) Amyotrophic lateral sclerosis (1) Disseminated sclerosis (1)
Jolliffe and Colbert[45]	Alcoholic polyneuritis	1	Borderline, adequate in thiamin	10	Intravenously	5		+			+		+	+	
	Alcoholic polyneuritis	1	Borderline, adequate in thiamin	10	Intravenously	14	18 gm. autoclaved Vegex*	+			+			+	
	Alcoholic polyneuritis	1	High-vitamin	10	Intravenously	9	18 gm. Vegex		0					+	
Sciclounoff and Broccard[46]	Alcoholic polyneuritis	1		1.5	Parenterally	26						+		+	Postdiphtheritic paralysis (2) Diabetic polyneuritis (5)
	Alcoholic polyneuritis	1		9, then 1.5	By mouth and parenterally	17		+				+	+	0	
	Alcoholic polyneuritis	1		1.5	Parenterally	6			+			+			
	Korsakoff's psychosis	1		1.5	Parenterally	11		"All symptoms cured"					+		
	Korsakoff's psychosis	1		1.5 6	Parenterally and by mouth	16		+				+			
Russell[47]	"Chronic progressive polyneuritis"	1		0.3 each third day	Parenterally	10 (?)			0	+			+	+	Combined system disease (2)
	Alcoholic polyneuritis	1		0.3 daily, then each third day	Parenterally	13 (?)				+		+		+	
Theobald[48]	Pregnancy polyneuritis	4		4.5–7.5	By mouth	10–21		+	+						
Desrochers and Larue[49]	Alcoholic polyneuritis	1	Reference not consulted												
Staehler[50]	Pregnancy polyneuritis	3		5	Intramuscularly	3	Cod-liver oil	+		+			+		
Spies and Aring[52]	Pellagra	2	Pellagra-producing	50	Intravenously	9 (?)–25		+			0	+	+	0	
Stevenson[53]	Nonspecific neuritis	27		1–2	Intramuscularly	14–21		+							
Goodhart and Jolliffe[54]	Alcoholic polyneuritis	8	High-vitamin	10	Intravenously	10	18 gm. Vegex	Objective signs showed more improvement than in control group of 9 cases on same diet and Vegex but without additional thiamin.							
Vorhaus[56]	Neuritis, all types	505		3–10	By mouth and parenterally			Improvement in symptoms (which symptoms not stated).							

+ = reported improvement; 0 = reported absence of improvement; blank space = no report. *Vegex is an extract of yeast, and a potent source of the entire Vitamin B complex.

of thiamin therapy in the treatment of the neuritides of diabetes, leprosy, metallic and other toxic poisonings, postdiphtheritic paralysis, combined system disease, disseminated sclerosis, tabes dorsalis, herpes zoster, trigeminal neuralgia, chorea and poliomyelitis. Reference to the use of thiamin in these conditions will be found elsewhere.[5, 39] This review will be limited to a discussion of the literature recently cited[1, 3, 39] as demonstrating the beneficial effect of thiamin in the treatment of polyneuritis of definite nutritional origin,* together with a few other references which are outstanding in their claim of the value of thiamin in the treatment of nonspecific neuritides, and therefore warrant careful analysis.

As Table 1 shows, the evidence for the cure of nutritional neuritis by thiamin therapy depends chiefly on the relief of symptoms. With the exception of the report of 3 cases by Jolliffe and Colbert,[45] there is only one attempt, that of Goodhart and Jolliffe,[53] to carry out a full analysis of the effect of this therapy in bringing about an alteration in the objective signs, both sensory and motor, of nutritional polyneuritis. These authors studied 17 patients with alcoholic polyneuritis whom they fed on a vitamin-rich diet supplemented by a potent source of the entire vitamin B complex (Vegex, an extract of yeast), in sufficient amounts to raise the estimated thiamin intake to four times the normal requirement. Eight of these subjects were given in addition 10 mg. of thiamin intravenously daily. After ten days of treatment the improvement in these patients was compared with that in the remaining 9, who received diet and Vegex only. Of those who received only diet and Vegex, 2 improved in motor signs and 4 showed sensory improvement, whereas of those who received additional thiamin, 5 showed motor and 8 sensory improvement. (It is noteworthy that from the protocols given by these authors it would appear that after another six days 1 more of the first group showed motor improvement, and 3 more sensory improvement.) There are certain difficulties in accepting these results as definite evidence that thiamin is capable of relieving nutritional neuritis. In the first place, a study of this kind, which compares the rate of improvement in two groups of cases in both of which recovery is taking place, is liable to error unless a large number of cases are studied. Secondly, the additional thiamin might have had some influence in improving digestive function and facilitating the absorption of other antineuritic factors present in the Vegex. Finally, the changes in physical signs observed must have been due to improvement in the function rather than in the structure of the nerves, since they took place in the short space of ten days, which would hardly be long enough to allow of much regeneration of degenerated nerve fibers.

Analysis of the remainder of the literature shows that in the majority of the other studies reported no mention has been made of the diet received by the patients. The possibility of other dietary factors contributing to the observed response cannot therefore be excluded. Furthermore, in several cases the doses of thiamin given were so small as to raise doubts whether its administration had any significant influence on the clinical course.

The evidence throughout rests mainly on the relief by thiamin of the symptoms of pain, weakness and inability to walk. Unpublished observations by myself, based on a study of 2 alcoholic patients with polyneuritis who were fed a vitamin B-free diet and received intramuscular thiamin without other medication, confirm the impression that thiamin may have a marked effect in the relief of muscle pain and tender calves in nutritional polyneuritis. But in these cases there was no associated improvement in the objective neurologic signs, and the relief of the pain cannot be taken as evidence of improvement in the neuritis. There seems to be good evidence for the belief that this pain has in fact little to do with the associated anatomic changes in the peripheral nerves. The character of this type of pain and its related symptoms have been described by Strauss[55] as follows:

> Heaviness of the legs and tenderness of the calf muscles when they are squeezed are usually the earliest manifestations. Walking short distances is unimpaired, but when longer walks are attempted weakness may become apparent. Frequently patients will note that they will commence walking with no disability whatever but that after having traversed a variable distance their legs will suddenly collapse under them. At first a distance of a mile or more may be required to bring out this weakness. Later a hundred feet may be sufficient. After some minutes of rest, walking can be resumed.

A similar description of this pain as it occurs in endemic Oriental beriberi has been given by Platt and Gin[56]: "Patients complain of severe aching pain in the legs after walking, the ease with which the pain is induced being some index of the severity of the disease. Moreover, the degree of recovery from beriberi can be estimated roughly in those cases without marked muscular atrophy by the distance they can walk before pain develops." These authors then add the following significant statement, "Our clinical observations taken

*One paper[49] which has been quoted[1,3] in illustration of the value of thiamin in the treatment of polyneuritis of pregnancy will not be reviewed here, since in the 2 cases described therein the patients apparently suffered from pain due to obstetric trauma rather than to polyneuritis.

together with the views expressed on the metabolic basis of the disease suggest that the mechanism of pain production is similar to that following ischemia described by Lewis and his collaborators." It is important to point out that thiamin is known to be concerned with the normal metabolism of carbohydrate, and that deficiency of this vitamin results in a disturbance in the normal path by which carbohydrate is broken down, and consequent accumulation of lactic and pyruvic acids in the tissues.[11] Since carbohydrate metabolism plays a very important part in providing the energy necessary for muscular work, deficiency of thiamin is probably as effective as partial anoxia in arresting the normal metabolism of muscle. I agree with Platt and Gin that the pain associated with true thiamin deficiency is primarily due to the same mechanism as that which produces ischemic pain, namely, the arrest of normal metabolic processes in the tissues. Thiamin by restoring these processes may relieve the pain, but this is no evidence that it relieves the anatomic changes in the peripheral nerves which may also be present. Neuritis may be a factor in the production of this pain only in so far as the threshold for pain is probably lowered in demyelinated nerves, and hence the disturbed metabolism of the tissues induces an abnormally intense response of pain receptors.*

It is noteworthy that Naide[59] has recently shown that the parenteral administration of large doses of thiamin sometimes relieves rest pain of ischemic origin. This observation may perhaps be explained on the ground that defective circulation hinders the normal supply of thiamin to the tissues, and that in this way their metabolism, which is already impaired by partial anoxia, becomes sufficiently disturbed to evoke pain. It is interesting to speculate whether impaired carbohydrate metabolism in diabetes mellitus may sometimes cause pain of an essentially similar nature, and whether such pain may contribute to the symptoms of diabetic neuritis. If this should prove to be the case, it is nevertheless unlikely that the administration of thiamin would relieve this pain, since the "biochemical lesion" in diabetes occurs at a stage of carbohydrate metabolism remote from the point at which thiamin is known to act. In conformity with this theory, it may be mentioned that in spite of some reports in the literature of the beneficial effects of thiamin in the relief of diabetic neuritis, apparently no leading authority on diabetes has yet expressed agreement with these reports.

In view of the foregoing considerations and from the analysis of the literature given in Table 1, the following statements from recent articles appear to be scarcely justified at the present time.

> The clinician was thus provided with a method of approximating the vitamin B_1 requirement of man, a knowledge of many factors modifying this requirement, and a therapeutic agent that could be administered *per os* or parenterally in pure form without incidentally furnishing other factors. With the use of these advances the clinician has been able in a period of three years to complete the evidence necessary to prove that many of the varieties of polyneuritis . . . are caused by vitamin B_1 deficiency. — Jolliffe.[3]

> The treatment of polyneuritis of beriberi has become highly successful since the introduction of concentrated and crystalline forms of the vitamin. — Wilbur.[4]

> Vitamin B_1 will usually relieve the manifestations of the polyneuritis of beriberi. — Spies et al.[57]

> The feeding of thiamin is followed by re-myelinization and a return to normal in the microscopic appearance of the nerve trunks. — Vorhaus.[54]

Certain proof that thiamin will cure polyneuritis can only be achieved by a carefully controlled study in which all other factors of the vitamin B complex are excluded from the diet and thiamin alone is administered. If one is to judge by what is known of the rate of regeneration of degenerated nerve fibers, — traditionally stated to be 1 mm. a day, — this experiment would have to be extended over a long period, and for this reason may never be undertaken.

It is perhaps unfortunate that physicians do not often report their negative results. If this custom were commoner, present beliefs in the efficacy of thiamin in the treatment of nutritional neuritis might be less prevalent. However, some disappointing results have been recorded (Ungley[60]). It is significant that apparently no optimistic reports have yet appeared on the use of thiamin in the treatment of the neuritis of endemic beriberi. A recent review from the Orient states, "Most workers seem agreed . . . that the results of treatment of peripheral neuritis are much inferior to the treatment of acute cardiac beriberi" (Pallister[61]).

It is concluded that there is at present no proof that thiamin has any influence in effecting repair of nerve fibers which have suffered from degener-

*In discussing the action of thiamin in the rapid relief of neuritic symptoms, Spies and his collaborators[57] have recently stated: "It is our thought that the initial prompt improvement with thiamin in cases of nutritional deficiency is humoral in nature. This impression is furthered by the work of Minz, who has been able to show that vitamin B_1 enhanced the effect of acetylcholine in the transmission of the nervous impulse. It seems that vitamin B_1 inhibits cholinesterase in the same manner as does physostigmine. In our cases in which this test was performed (in vivo) the serum cholinesterase was inhibited by the administration of thiamin."

It is noteworthy that Minz[58] specifically states that this alleged action of vitamin B_1 is not explicable by an inhibition of esterase, but is due to an intensification of the effect of acetylcholine on the cell. Apparently Spies and his collaborators have evidence to the contrary, and for this reason the publication of their experimental data will be awaited with interest. Yet it is difficult to see how excessive acetylcholine destruction can have much to do with the production of pain.

ation as a result of nutritional deficiency. However, there is evidence that thiamin relieves a certain type of pain and disability which, though frequently associated with peripheral neuritis, is primarily due to a different cause. This pain is usually most severe in the muscles of the legs, particularly after exercise, and is quite distinct from the symptoms which are primarily due to neuritis. The cause of the pain is a disturbance of function rather than of structure; it is brought about by a disordered or pathologic metabolism.

Comment

Present beliefs concerning the relation of thiamin deficiency to the causation of nutritional polyneuritis are based on a misunderstanding between clinicians and laboratory workers. By long-standing tradition, laboratory workers have referred to the condition produced in animals by thiamin deficiency as polyneuritis. But they now know that there is no true peripheral neuritis in these animals, the physical signs being due to a disturbance of metabolism in the central nervous system. This disturbance is also present in other organs of the body, but it so happens that there it gives rise to no obvious external manifestations. The dramatic nature of the nervous signs and their spectacular relief by the administration of thiamin have given rise to the erroneous belief that thiamin plays a peculiar and specific role in the nutrition of the nervous system. And so it has come about that the vitamin has usurped the title of "antineuritic vitamin," which it in no way deserves. There is no definite proof at present that thiamin deficiency produces in animals the anatomic changes of a true peripheral neuritis, and certainly no evidence that thiamin will cure the peripheral neuritis produced in animals by other deficiencies.

In view of this misunderstanding,—the responsibility for which is shared by myself,—it is not surprising that when synthetic thiamin became available, clinicians were misled into thinking that this was the antineuritic vitamin which would cure nutritional neuritis in animals and presumably also in man. Perhaps this error might have been pointed out by the laboratory workers had it not been for the fact that very optimistic reports of the clinical value of thiamin in human nutritional neuritis soon began to appear. The laboratory workers, accepting the judgment of clinicians in clinical matters, were gratified to learn that thiamin relieved polyneuritis in man, although they had no evidence that it did so in animals.

Meanwhile the reports of clinicians were being founded on the fact that thiamin appeared to relieve the pain and weakness associated with nutritional polyneuritis. However, there is reason to think that these symptoms are not primarily due to the neuritis, but to the same fundamental cause that gives rise to the nervous signs in animals, namely, a disorder of carbohydrate metabolism. As a result, both laboratory workers and clinicians have concluded from a similar misinterpretation of different evidence that thiamin will cure the anatomic lesions of polyneuritis.

When the literature of the last ten years is considered in perspective, the conclusion is inescapable that thiamin has never deserved the title of "antineuritic vitamin," and has not yet shown itself capable of filling completely the role that was formerly assigned to the hypothetical antiberiberi vitamin.

The exact deficiency responsible for nutritional neuritis remains obscure. Quite probably it is usually a multiple deficiency involving several dietary factors, of which thiamin may be one. But there is still a possibility that the true antineuritic vitamin has yet to be discovered.

Conclusion

The polyneuritis associated with alcoholism, pregnancy and gastrointestinal disturbances is unquestionably due to nutritional deficiency, and is in every way similar to the polyneuritis of Oriental beriberi. But, contrary to numerous statements in recent literature, it has not been demonstrated that this polyneuritis is due to deficiency of thiamin.

For this reason it is of paramount importance that the treatment of nutritional polyneuritis should include an ample and nutritious diet, together with the administration of such preparations as yeast and crude liver extract to ensure an adequate supply of the entire vitamin B complex. The efficacy of this treatment has been established by sound clinical experience. Sometimes additional thiamin is beneficial, particularly in the cure of the cardiovascular disturbances of beriberi, and in the relief of the muscular pain and weakness which frequently accompany nutritional polyneuritis.

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OBSERVATIONS ON PRURITUS ANI*

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PRURITUS ani is one of the most distressing conditions involving the anal region, and the least amenable to treatment. This paper offers no new remedy, but describes the various treatments tried in 175 cases seen during the last four years at the Rectal Clinic of the Massachusetts General Hospital.

ETIOLOGY

The exact etiology of pruritus ani is not definitely established. There are many theories, but not one of them explains all the facts. Local pathologic conditions such as fissure, fistula, hemorrhoids and cryptitis, allergic manifestations, reflex phenomena from a distant irritative focus, products of decomposition such as indole and skatole, fungous or local bacterial infection and dietary intolerance — each of them, singly or in combination with others, has been considered the true etiologic factor. In most cases there probably are several factors. The anatomic distribution of the lesions of pruritus ani suggests that the offending agent comes out of the anus in the form of a liquid or gas, and probably comprises one or more of the by-products of normal or defective digestion. In support of this theory is the presence of redness and burning of the perianal skin after several loose bowel movements; this undoubtedly results from the action of strong digestive juices from the upper intestinal tract that have reached the anus before their chemical nature has been altered. The acute skin irritation observed around most ileostomy and some colostomy openings is due to the same factor. Acute perianal dermatitis with itching occurring after anorectal operation is another example; the offending agent in this type of case is an irritating discharge from the infected wound. It is possible that the sensitivity of the skin varies in different patients and that only those with pronounced sensitivity develop pruritus. Many patients at the Rectal Clinic stated that itching started with the passage of feces or even flatus. A woman patient discovered that, although she had no visible discharge from the anus, if she kept her menstruation pad fastened tightly against the anal orifice she remained free from pruritus, whereas if she did not do so itching invariably occurred. In this case it seems probable that the absorbent material of the pad took up the offending agent and prevented it from remaining in contact with the skin. In well-established cases, the leathery redundant skin folds at the anal margin prevent efficient closure of the orifice and undoubtedly allow constant seepage.[1] Mechanical irritation due to scratching and subsequent infection aggravate the condition. Local pathologic conditions such as fissures, cryptitis and hemorrhoids were present in 40 per cent of our cases. In numerous cases, however, the coexisting disease was corrected without relieving the pruritus or improving it permanently.

SYMPTOMS

Symptoms vary from the burning of an acute dermatitis, associated with erythema of the perianal skin, to a constant itching, in chronic, intractable cases. Erythema, vesiculation and excoriation are often seen superimposed on a thick leathery skin. Remissions of itching are common. For no apparent reason, several months or years may pass without any itching, and skin changes may disappear only to return again at some future date.

STATISTICAL REVIEW

The age of the patients in this series varied from eighteen to eighty. There was only 1 below twenty, while the third, fourth, fifth and sixth decades were about equally represented. Table 1 shows the age incidence in 155 cases. The ratio of men to women was almost 2:1. The reason for this we consider to be the more scrupulous hygiene which women patients employ after defecation.

TABLE 1. *Age Incidence (155 Cases).*

AGE yr.	NO. OF CASES
Below 20	1
20 to 30	30
30 to 40	38
40 to 50	35
50 to 60	34
60 to 70	14
70 to 80	3
Total	155

The duration of symptoms varied from one week to thirty years, as is shown in Table 2.

There was local disease in 40 per cent of the cases. This consisted chiefly of internal hemor-

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rhoids and external skin tags. Table 3 shows the various accompanying conditions found in 140 cases. Itching of the skin in other parts of the body was present in 19 of the 175 patients.

TABLE 2. *Duration of Symptoms (138 Cases).*

PERIOD	NO. OF CASES
Below 1 mo.	8
1 to 6 mo.	17
6 to 12 mo.	25
1 to 2 yr.	21
2 to 5 yr.	31
5 to 10 yr.	24
10 to 20 yr.	9
20 yr. and over	3
Total	138

The vulva and labia were involved in 11 cases, the pubes, thighs, groin or scrotum in 6. One patient had hay fever and 1 generalized dermatitis venenata.

TREATMENT

There is no specific treatment for pruritus ani. Each case should be treated individually by one method or a combination of several. Scrupulous hygiene is of paramount importance. This includes

TABLE 3. *Concomitant Disease (140 Cases).*

CONCOMITANT DISEASE	NO. OF CASES
Internal hemorrhoids	31
External tags	10
Fissure	5
Atonic sphincter	2
Fissure and hemorrhoids	2
Fistula and tags	1
Fistula and hemorrhoids	1
Infected crypts	2
Melanosis coli	1
Diverticulosis and hemorrhoids	1
None	84
Total	140

washing with soap and warm water after every bowel movement, and thorough drying without excessive rubbing.

Local Applications

For topical applications the following medicaments have been tried:

Calamine lotion
Hamamelis water (witch-hazel water)
Boric acid ointment
Salicylic acid and sulfur ointment (6 per cent each) in petrolatum
Castor oil (12 per cent), zinc oxide (18 per cent) and phenol (1 per cent) in lanolin
Nupercaine ointment, 1 per cent
Obtundia cream
Scott's solution
Tincture of Metaphen
Tincture of benzoin
Silver nitrate, 10 per cent
Resorcinol (2 per cent), benzoic acid (2 per cent) and thymol (1 per cent) in alcohol (95 per cent)

These various medicaments are either soothing, astringent, antiseptic, keratolytic or anti-pruritic. Most cases respond to one or another.

Many simple early cases can be cured with nothing more than careful hygiene. Acute stages of erythema, excoriation and vesication without chronic skin changes can be made to disappear in one or two weeks by the application of Scott's solution or Tincture of Metaphen daily. Even cases that present signs of an acute dermatitis superimposed on chronic skin changes should be so treated. In the chronic cases showing thickening and discoloration of the skin without superimposed acute irritation, keratolytic and antipruritic ointments should be used. The application of salicylic acid and sulfur ointment is effective. With good hygiene, and by continued use of this or a similar ointment, improvement may be rendered permanent.

Injection Treatment

When all simple treatments fail, that is, hygiene, astringent and antiseptic lotions and keratolytic and antipruritic ointments, we resort to some form of subcutaneous injection in order to interrupt the afferent sensory pathways. It was necessary to use injection treatment in 48 cases. Eighteen cases were injected with a solution containing quinine and urea hydrochloride and novocain. Sixteen were injected with an oil-soluble anesthetic, and 14 with alcohol. No injection treatment should be carried out in cases with acute exacerbations.

Quinine and urea hydrochloride. Eighteen cases were injected with a solution containing quinine and urea hydrochloride, 0.75 per cent, and novocain, 0.175 per cent.[1] The entire perianal area was treated at one sitting. The solution was injected subcutaneously through two punctures, one on each side 4 cm. from the anal margin, 10 to 15 cc. of the solution being used for each side. Only partial relief was obtained, but even this result was quite satisfactory to the patient. Anesthesia usually lasted for three or four weeks, while 3 patients experienced partial relief for as long as six months. In 2 cases with acute exacerbations no relief was obtained. Injection was repeated in a few cases, but after the third or fourth injection there was so much fibrosis beneath the skin that further injections were almost impossible. There was no sloughing in any of the cases, and there were no painful reactions.

This type of treatment did not seem to be very effective.

Oil-soluble anesthetic. Sixteen cases were treated by injection of an oil-soluble anesthetic. The solution used was that recommended by Gabriel,[2] consisting of 0.5 per cent Nupercaine, 10 per cent benzyl alcohol and 1 per cent phenol in oil of sweet almonds. Under aseptic precautions, the oil was injected subcutaneously by means of a 10-cc. Luer-Lok syringe and a 22-gauge needle, 1½ inches long. Either one or two quadrants were injected at weekly intervals, using about 5 cc. of oil for each quadrant. One slough took four weeks to heal. The immediate results were very satisfactory on account of the almost complete anesthesia obtained. On the average, relief was complete for three weeks and partial for two or three weeks longer, after which recurrence invariably took place. Marked subcutaneous fibrosis occurred after three or four weeks, making a second attempt to inject oil almost impossible. This gradually disappeared after three or four months.

Alcohol. Fourteen cases were injected with 70 per cent alcohol as described by Haskell and Smith.[3] One quadrant was treated at a time at weekly intervals. All the patients were ambulatory. The perianal area was washed with soap, dried and painted with Scott's solution or Tincture of Metaphen. The quadrant to be treated was infiltrated subcutaneously with 2 per cent novocain through a 26-gauge needle puncture 4 cm. from the anal margin. Five cubic centimeters of novocain was used and massaged thoroughly to diffuse the solution in order not to dilute the alcohol. The novocain must be injected well beyond the limits of the proposed alcohol injection in order to ensure complete anesthesia. Through the same needle puncture 3 to 5 cc. of alcohol was injected, taking good care to distribute the solution evenly and thus to prevent pooling. The alcohol should be injected into the subcutaneous tissue. If at any point it is injected into the skin, necrosis is sure to occur. There is considerable burning, which may last several hours after the wearing off of the novocain anesthesia. This is relieved by hot packs. There is redness and induration for a few days. A slough is to be expected in one out of four injections, but it usually consists of nothing more than a small area of skin necrosis. This should be allowed to heal before further injection is attempted.

Our results were satisfactory in 7 out of 10 cases. In 4 cases only two quadrants were injected. Three of these patients did not return. This may mean either that they had complete relief or that they had much pain and were afraid to return. The fourth patient appeared one year later with itching in the quadrants not previously injected. Of the 10 cases in which the injection of the perianal skin was complete, 5 followed for over a year showed satisfactory results. These patients had anesthesia for two or three months. All had occasional itching after three months, but it was very mild compared with what it had been before. All the patients stated that their itching was only 10 to 15 per cent of its previous intensity. One other patient was followed four months, and was well at the end of that time. Another was followed only two months and was symptom-free. One case recurred at the end of four months. Two cases were complete failures; one had previously been injected with alcohol, and the other with Gabriel's solution. The patients obtained relief for only a few weeks.

X-Ray Treatment

Of the 4 patients treated by x-ray, 1 obtained relief for seven weeks, 1 for three weeks, 1 had no relief and 1 had partial relief for a year.

Conclusions

Each case of pruritus ani should be treated as an individual problem. Most of the early cases do well with carefully regulated hygiene and soothing lotions. Chronic cases with acute exacerbations improve when painted with Tincture of Metaphen or Scott's solution. The acute dermatitis clears up in one or two weeks, and good hygiene prevents a recurrence in many cases. In chronic cases with skin thickening, keratolytic or antipruritic ointments are often sufficient. In about one fourth of our cases all simple treatment failed and some form of injection was necessary. Subcutaneous injection of 70 per cent alcohol gave the best results in this group.

Summary

The etiology of pruritus ani is discussed.

Statistics on 175 cases are given.

The various forms of treatment are summarized.

Results of the injection of quinine and urea hydrochloride and novocain, Gabriel's solution and 70 per cent alcohol are reported.

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THE TREATMENT OF GONOCOCCAL INFECTION IN WOMEN*

A Comparison of the Results with and without Sulfanilamide Therapy

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GONOCOCCAL infection in women is more widespread and a far more serious infection than it is in men. Its complications, sterility, obstinate infection and invalidism, are responsible for a major part of the work of the gynecologist. Gonorrhea occupies a unique position among acute infectious diseases, not only in its clinical manifestations but in the fact that the organism, the gonococcus, has certain special inherent characteristics that differentiate it very conspicuously from other pathogenic bacteria. There exists no immunity to the gonococcus, either from previous infection or by individual resistance or racial qualities.

The gonococcus has a selective action for certain mucous surfaces, and when deposited on these grows immediately and profusely in the same manner as do other bacteria on their favorite soil. No injury to the surface of the tissue is necessary for its growth and reproduction. The organism is exclusively a human parasite, and is with difficulty grown on species other than man. The gonococcus is sensitive to both heat and cold, and is very fragile out of its normal or cultural environment. In the presence of other bacteria in a culture the diplococcus is readily crowded out. From a clinical standpoint one of the unusual peculiarities of a gonococcal infection is its power of latency. The organism can remain in the tissues for months in an apparently dormant state until stimulated into activity by some change in the circulation in the surrounding tissue. This renewed activity can be produced by local trauma, childbirth, menstruation, pelvic operation, excessive venery or systemically by some other infection or by alcohol. The exacerbation of a chronic infection may present all the symptoms of a fresh invasion. For the development of a gonococcal infection the tissue on which the organism is deposited must be of special epithelial structure; it must be moist and the blood supply abundant. The tissues most frequently invaded are those of the urethra, Skene's glands, cervix, Bartholin's glands, fallopian tubes, peritoneum, rectal mucosa and the conjunctiva.

During the eight-year period 1930–1937 we used in the treatment of gonococcal urethritis and cervicitis local instillations of 1 per cent silver proteinate in a 4 per cent gelatin mixture. This was given each day for two or three weeks. We are of the opinion that by the addition of gelatin to the medicament the drug is held in closer contact with the tissue — a surface-tension phenomenon. The gelatin seems to possess the power to take up the toxic products, — exotoxins and endotoxins, — and in this manner to diminish the irritating quality of the discharge and at the same time presumably increase the beneficial action of the drug. Oral medication consisted of the ingestion of 10 minims of sandalwood oil three times a day after meals. Patients with a concomitant rectal infection were given suppositories containing 1 per cent silver proteinate in oil of theobroma. These were inserted following each bowel movement. In patients who had suffered a pelvic extension, rest in bed, application of heat to the lower abdomen and intramuscular injections of a foreign protein were productive of good results. At the first sign of pelvic involvement, which usually occurs at about the time of the menstrual period, all local treatment was discontinued and vaginal examinations were omitted. Douches were not prescribed at any stage of the infection, as they do little good at any time and may be distinctly harmful.

We have reviewed 241 case records of patients treated by this method. In this series 230 patients were Whites and 8 were Negroes. One hundred and one were married, 32 divorced, 21 separated, 8 widows and 79 single. The youngest patient was sixteen years of age, and the oldest fifty-two. The average age was twenty-eight. Forty-six patients gave a history of a previous gonococcal infection.

The tissues found to be infected are shown in Table 1. The infection if primary in the urethra was rarely limited to this site, and the reverse was true of cervical involvement. In many cases more than one area was involved at the time of admission.

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‡Staff member, Gynecological Department, Public Health Institute.

One of the most distressing complications of gonorrhea in women is extension to the fallopian tubes. Despite any and all forms of treatment, the number of women suffering from this invasion is large. There were 92 patients, or 40 per cent, in this group who had a salpingitis, in 10 of whom it was present on admission. There were 15 patients who developed an infection of Bartholin's gland. None of these infections were bilateral. Only 2 patients had an arthritis, and in both cases the sexual partner suffered the same complication. In this connection, having observed a number of similar cases we have concluded that the condition may be due to a special strain of the gonococcus which has a selective affinity for the articular surfaces of the joints. We never apply a splint or cast in these cases, and in only 1 case has there been any loss of joint function, due in this case to lack of co-operation by the patient.

TABLE 1. *Infected Tissues in 241 Cases Treated without Specific Chemotherapy.*

INFECTED TISSUE	NO. OF CASES
Urethra	173
Cervix	193
Rectum	96
Bartholin's gland	15
Tubes	92
Joints	2

The uncomplicated cases were under treatment or observation for an average of one hundred and one days, with an average of thirty-five visits for treatment and observation. The average length of time before the vaginal smears became negative and remained so was ninety-seven days. Seven weekly smears were examined before the patients were dismissed.

In the group of patients who had a pelvic infection the average period of treatment was one hundred and thirty days, and an average of ninety-seven days elapsed before a negative smear was obtained. While the average number of weekly observation smears taken in the cases without complications was six, the number in the cases of salpingitis was nine.

In taking smears as criteria of cure we secure at least two before and at the completion of a menstrual period. All treatment procedures are omitted when these tests are being made. After a patient is dismissed from treatment we urge her to refrain from sexual intercourse for at least three months, but direct that should she expose herself all possible precautions are to be taken before and after the act. All patients are advised to return in three months for a re-examination. Ninety-six patients (40 per cent) did so, and all were found to be free of gonorrhea.

In a group of 241 cases in which the patients received the same local therapy but were given sulfanilamide orally, there were 230 Whites and 11 Negroes. Seventy-eight were married, 32 divorced, 32 separated, 17 widows and 82 single. The youngest was seventeen and the oldest fifty-one. The average age was twenty-seven. There were 25 patients who admitted a previous gonococcal infection.

The tissues found to be infected are shown in Table 2. A large number of patients had the infection in the urethra and cervix at the time of admission. Gonococci were found in the rectal smears in 97 cases. Gonococci were only rarely isolated from the rectum without organisms' being found in the urethra or cervix or both. There were only 32 patients (13 per cent) with a salpingitis, an incidence which is nearly three times less than that in the group treated by the older method. The infections of Bartholin's gland in this group were double the number found in the previous series; however, we cannot explain this finding.

TABLE 2. *Infected Tissues in 241 Cases Treated with Specific Chemotherapy.*

INFECTED TISSUE	NO. OF CASES
Urethra	156
Cervix	152
Rectum	97
Bartholin's gland	22
Tubes	36
Joints	1

The uncomplicated cases were under treatment and observation for an average of sixty-five days. This represents an improvement of about 35 per cent when sulfanilamide is administered. The average length of treatment and observation for the complicated cases was seventy days, an improvement of almost 50 per cent in comparison with the first classification (Table 3). One of the surprising phenomena noted was that the patients who were able to take only 20 gr. of sulfanilamide daily made almost parallel progress with those

TABLE 3. *Comparison of Results with and without Sulfanilamide Therapy.*

DATA	METHOD OF TREATMENT	
	WITHOUT SULFANILAMIDE	WITH SULFANILAMIDE
Average number of days under treatment and observation:		
Uncomplicated cases	101	65
Complicated cases	130	70
Average number of treatments before smears remained negative	28	17

taking larger doses. We have no satisfactory explanation for this observation, unless it be that the concentration of the drug in the blood has not the significance previously attributed to it in relation to the control and cure of gonorrhea. Forty-two patients (17 per cent) were unable to take sulfanilamide in doses of any size. In 29 of these cases the medicament was omitted from the treatment plan, as the reactions were of sufficient severity to interfere with the occupation of the patient. In 5 cases the drug caused a dermatitis which was not dangerous but was very disturbing to the patients. In an additional 45 cases the dosage was reduced from 40 to 20 gr. daily without the elimination of annoying reactions.

Summary and Conclusions

This study purports to show that the modern management of gonococcal infection in women with sulfanilamide and topical applications halves the distressing pelvic complications and reduces the length of time of treatment by a third. We observed an increase in the number of abscesses of Bartholin's gland, but can give no satisfactory explanation for this finding. However, the complication is of minor importance in so serious an infection. The reactions to sulfanilamide are numerous but usually of a minor nature. Seventeen per cent of the patients were unable to take 40 gr. of the drug without disturbing reactions.

159 N. Dearborn Street

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FORTY-NINTH ANNIVERSARY

House of Delegates, May 13, 14 and 15, 1940

(Continued from the issue of July 25)

Report of the Committee on Medical Economics

The Committee on Medical Economics has given its consideration to three problems during the year.

Farm Security Administration Insurance Program. In pursuance of the instructions given it by the House of Delegates at its annual meeting, your committee studied the proposals of the Farm Security Administration relative to health insurance for its clients, and made recommendations for the guidance of any county societies contemplating the plan. These recommendations were transmitted to the several county secretaries.

The program for general-practitioner care is now in operation in Grafton and Cheshire counties, having gone into effect January 1, 1940. The Sullivan County Society at first approved the proposals, but later rescinded its action and withdrew from the plan. Obviously the length of time that the plan has been in effect is too short to justify any conclusions regarding it.

Sickness Insurance. Because of the widespread interest among lay, governmental and medical circles in the problem of the distribution of medical care, and because of the particular emphasis among members and groups of the profession in some form of insurance as an answer to the problem, your committee has begun a study of this question.

The intricacies and complexities of the problem are manifold, as attested by the large number of differing plans which are now in operation under the supervision of state and county medical societies, and by the long and expensive investigations conducted by several state societies before any satisfactory conclusions could be reached.

Your committee is not prepared to make any recommendations regarding sickness insurance in New Hampshire. It does recommend that the study be continued, with a view to observing the operation of the various plans now in effect and for the purpose of drawing up a plan which would be applicable in New Hampshire if the need should arise.

National Physicians' Committee for the Extension of Medical Service. Your committee believes that the solving of the problem of the adequate distribution of medical care is of urgent and vital importance. It further believes that the National Physicians' Committee for the Extension of Medical Service is composed of able and upright leaders of the profession who are making a vigorous attack on this problem.

Your committee, therefore, recommends that the House of Delegates approve the activities of the National Physicians' Committee for the Extension of Medical Service and urge its members to accord this committee their active moral and financial support.

Leslie K. Sycamore,
Richard W. Robinson,
Clarence E. Dunbar.

Dr. Robertson: The Committee on Officers' Reports recommends that this committee's recommendation, with respect to the continuation of the study of sickness insurance, be adopted.

We further approve the recommendation relative to the National Physicians' Committee for the Extension of Medical Service, and recommend that this action be reported to that committee and to the members of the Society, urging their active, moral and financial support.

I move the adoption of this portion of our report.

This motion was seconded and was carried.

Report of the Committee on Tuberculosis

The program for the control of tuberculosis has progressed to the point where our goal at this time is to conquer the disease so completely that it will be eradicated from the human family. Eradication is not now a hoped-for possibility but an actuality which can be won, in the considered judgment of leaders in preventive medicine throughout the nation. Sound basis for this conclusion is the tremendous progress already gained in the control of the disease, the increasing effectiveness of treatment, and the definite resources available for early discovery of cases.

Our greatest difficulty today, as in the past, is to find the people who have tuberculosis. Eighty per cent of the patients admitted to the New Hampshire State Sanatorium during the past year were moderately advanced or late cases.

This vital phase of the campaign against the disease — the finding of the people who have tuberculosis — has grown in the past twenty years. Two important developments give additional encouragement to physicians, public-health workers and others engaged in the task. The first — the tuberculin test — tells us whether or not a person is infected with tubercle bacilli. The second — x-ray study of the chest — demonstrates early pulmonary lesions. We urge that the tuberculin test and x-ray study of positive reactors be accepted and carried out as a routine procedure in hospitals and in general practice.

Your committee again reminds you of its willingness to be of service in the matter of interpretation of chest x-ray films sent in for readings.

The Vollmer patch tuberculin test is now being used in the tuberculosis clinics as a routine procedure. The comparative studies made so far as to the relative reliability of the patch test and the standard intradermal protein-purified-derivative (P.P.D.) test indicate that the former is equal to the latter in its effectiveness as a diagnostic index of the presence or absence of tuberculous infection. Of 6000 comparative testings reported in the studies throughout the country, New Hampshire reported 1455. The intradermal test is still being used in the tuberculin-test and chest-x-ray demonstrations conducted by the New Hampshire Tuberculosis Association among the high-school groups. However, in the regular diagnostic clinics the patch test is used.

We realize that the cost of treatment of tuberculous patients has increased because of the increase in the use of surgery in treatment, and that the cost of the discovery and prevention of tuberculosis has increased because of the necessary employment of tuberculin tests and chest x-rays. We emphasize here, however, as no doubt we have in previous reports, that an adequate investment now to speed up and hasten the control of tuberculosis will be self-liquidating and final.

ROBERT B. KERR,
ROBERT M. DEMING,
JOHN D. SPRING.

DR. ROBERTSON: The Committee on Officers' Reports urges the physicians of New Hampshire to use the tuberculin test more freely.

I move the adoption of that portion of our report.

This motion was seconded and was carried.

Report of the Committee on Child Health

Your committee held scheduled meetings on September 1 and November 10, 1939, and March 16 and May 3, 1940.

Last year we stated that the *Report of the Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases* of the American Academy of Pediatrics, for which we had received an appropriation of $50, was out of print. This year a revised, larger report was printed, and this was sent to each member of the Society. Your committee endorses wholeheartedly the recommendations of the committee of the American Academy of Pediatrics.

Subsequent experience is bearing out the value of tetanus toxoid, particularly for people who are allergic and therefore not good subjects for horse serum. We believe that this should be used more widely, either plain or mixed with diphtheria toxoid.

We previously reported an interest in the health standards of summer camps. We note with approval that the Department of Health has ruled that only pasteurized milk may be used in these camps.

Your committee has continued to work in close cooperation with the Division of Maternal and Child Health and the State Board of Health. The following activities were carried out by the Division of Maternal and Child Health and the Division of Crippled Children at the suggestion and with the help of your committee:

1. A consultation service utilizing two pediatricians appointed by the State Board of Health was instituted during the fiscal year. The duties of these consultants are as follows: to serve local physicians by acting as consultants on pediatric problems; to evaluate the conduct at existing child-health conferences and to aid in the setting up of conferences; to advise in the selection of literature on subjects of child health for free distribution to the public; to aid in the teaching program to lay and professional groups concerning matters of value in problems of child health and pediatrics; to conduct teaching child-health conferences; to evaluate and aid in the working out of conference forms, such as records, at child-health conferences; and to carry out such other advisory services in the field of child health as may be presented.

2. The library of educational films dealing chiefly with subjects of child health and child behavior has been enlarged. The recent purchase of the film "Life Begins" had the endorsement of the committee.

3. Increased activities were carried out in the educational program by extension to lay groups of talks concerning the value of breast feeding, nutrition of the child and helpful points concerned with infant feeding.

4. Efforts to use the two-dose toxoid in the immunization against diphtheria in preference to the one-dose alum precipitate and the discontinuation of performing Schick tests, except in certain special cases, were adopted as a policy.

5. Wider free distribution of silver nitrate to local physicians and to hospitals for use in the eyes of the newborn was recommended.

6. The utilization of pediatricians at crippled-children's clinics, to ensure better care of the child and a general health appraisement, was advised.

7. Wider free distribution of vaccines, especially smallpox vaccine, to physicians requesting them was recommended. This is in line with our previous rec-

ommendation in attempting to facilitate the practice of preventive medicine in the office of the doctor instead of having all people in the low-income group of necessity availing themselves of free clinics.

The advice of your committee was helpful in the preparation by the Department of Health of the pamphlet on summer camps. We were able to bring to the attention of the department the work of some of the members of the Academy of Pediatrics along this same line.

Your committee has again endeavored to keep in the closest possible touch with progress in pediatrics by attendance of individual members at regional and national meetings of the American Academy of Pediatrics, through representation on the council of the New England Pediatric Society and by attendance at meetings of the national public-health organizations.

COLIN C. STEWART,
TRAVIS P. BURROUGHS,
FRANKLIN N. ROGERS.

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DR. ROBERTSON: The Committee on Officers' Reports moves the adoption of this report.

This motion was seconded and was carried.

Report of Necrologist

The following deaths have occurred during the past year:

1939

NAME	PLACE OF DEATH	DATE
Walter A. Allen	Haverhill, Massachusetts	August 23
Lloyd H. Cogswell	Warner	November 25
Charles F. Flanders	St. Petersburg, Florida	November 12
Bert D. George	Rochester	May 21
Alpha H. Harriman	Laconia	May 30
Elmer E. Lake	Hampstead	December 6
Alfred A. Macleavy	Manchester	June 1
John J. Mulvanity	Boston, Massachusetts	August 13
H. Scott Pattee	Manchester	August 26
Guy D. Tibbetts	Antrim	June 2

1940

Alfred Bielschowsky	Brooklyn, New York	January 5

HENRY H. AMSDEN.

DR. ROBERTSON: I move the acceptance of this report of the necrologist.

This motion was seconded and was carried.

DR. CHESTER L. SMART: We have received a communication from the Joint Committee on Professional Relations, which includes the Medical Society of New Jersey and the New Jersey Pharmaceutical Association. This letter was with reference to a resolution which was sent to us last year, but which was not acted on. The resolution is as follows:

RESOLVED: That the Joint Committee on Professional Relations request the Medical Society of New Jersey and the New Jersey Pharmaceutical Association to enter a formal protest against the prescribing of medicines and the giving of medical advice on the radio, with the exception of such broadcasts on health matters as are given under the auspices of recognized associations of licensed physicians or federal, state and local health departments; and be it further

RESOLVED: That such protest be sent to the broadcasting companies and the Federal Communications Commission.

DR. ROBERTSON: Your committee recommends the adoption of this resolution.

This motion was seconded and was carried.

DR. DUBE: I have a communication from the Works Progress Administration, and the following recommendations are made:

1. That the Society approve the paragraph relative to injury cases requiring medical treatment. ("Injury cases requiring medical treatment shall be distributed among qualified physicians in as equitable a manner as possible. Injured employees may indicate their personal preference as to physicians and such preferences may be honored where the physician is qualified and the selection will not materially disturb the equitable distribution of cases among available physicians.")

2. That we believe these cases are equitably divided now.

3. That it is inadvisable and financially impracticable at this time for the New Hampshire Medical Society to have a committee or individual make monthly surveys and reports to the Works Progress Administration at Washington, D. C.

I move the adoption of these resolutions.

This motion was seconded and was carried.

DR. SMART: The University of New Hampshire is having its seventy-fifth anniversary next year.

DR. BLOOD: I move that the Society accept the invitation to co-operate, and that a committee of three, one of whom shall be the president, be appointed to confer with the University.

The motion was seconded and was carried.

DR. SMART: I move that Dr. Blood, Dr. Wilkins and the incoming president be the ones to confer with the University of New Hampshire.

The motion was seconded and was carried.

DR. SMART: We have a final communication here on the medical emigrés.

I move that the President, the Secretary and the three other members of the Public Relations Committee consider and be given power to act on this communication.

This motion was seconded.

DR. DEERING G. SMITH: You say "power to act"; does it mean that these men can recommend or not recommend? I think it would be much safer to table the whole thing. The present state law takes care of new applicants.

The motion before the House was withdrawn.

DR. SMART: I move that the matter of medical emigrés be tabled.

This motion was seconded and was carried.

DR. HENRY O. SMITH: The Trustees of the New Hampshire Medical Society present a recommendation for action by the House of Delegates. That recommendation is made by unanimous vote.

The Board of Trustees of the New Hampshire Medical Society recommends to the House of Delegates that the sum of $2000 be given to the trustees of Dartmouth College, to be used in helping defray the costs of sorely needed equipment for the medical school, this amount to be taken from the accumulated income of the Bartlett Fund, which can be used only "for the benefit of medical science."

DR. FREDERIC P. LORD: I second that motion.

DR. SMITH: For the information of any of the members of the House of Delegates who may not be familiar with the facts, let me make a brief statement.

The will of Dr. Josiah Bartlett, Jr., probated one hundred and two years ago this month, gave to the New Hampshire Medical Society the sum of $200, to be placed at interest for ten years, and "the product of which, with the original sum, to be a permanent fund, the annual income to be expended for the benefit of medical science as may be directed by a vote or votes of said society."

But one gift has been made from the income of this fund, now amounting to over $6000—a grant of $1000 made thirty-six years ago to aid in the construction of a new building for the Dartmouth Medical School. This school now urgently needs additional facilities for the departments of physiology and pathology, and it seems to me very fitting for this society to take the initiative in meeting this need.

Drs. Josiah Bartlett, Sr., Josiah, Jr. and Josiah, 3rd, all served as presidents of this society; Josiah, Jr., the donor of this fund, for seven consecutive years. Their connection with the Dartmouth Medical School is evidenced by the fact that to each one Dartmouth College granted the degree of M.D.

I believe that in no way can we more fittingly honor the memory of Dr. Josiah Bartlett, Jr., than by the grant of this sum from the income of the fund left to us by him.

The motion was carried.

DR. DEERING G. SMITH: I have a resolution in the matter of the increasing activities of state laboratories.

WHEREAS, The continued growth and development of that special branch of medicine known as clinical pathology is necessary for the proper diagnosis and treatment of the sick and is essential to the science and practice of medicine; and

WHEREAS, The growth of laboratories of state boards of health has been abnormally augmented by grants-in-aid from the Federal Government; and

WHEREAS, The effect of these grants-in-aid is to extend these services to all citizens without regard to their ability to pay; and

WHEREAS, The excessive development of laboratory medicine by state boards of health serves as an entering wedge for state-medicine practice, which apparently will include all medical specialties; and

WHEREAS, These practices will inevitably result in the curtailment of the practice of clinical pathology, which is essential for the continued growth and development of clinical pathology, and tend to discourage young, well-trained physicians from entering this essential field; be it therefore

RESOLVED, That the House of Delegates recommends to all state medical societies that they hold conferences with the authorities of the state boards of health with the view of limiting the services offered by the laboratories of these organizations (in general, laboratory services by the state board-of-health laboratories should be confined to requests made by health officers or others in authority representing municipal, township, county and state public-health and welfare organizations, and to requests made by physicians whose patients find it difficult or impossible to pay for the cost of laboratory services of this kind in the customary manner; in general, laboratories of the state boards of health should not provide services at taxpayers' expense to persons who are able to provide for themselves); and be it further

RESOLVED, That the House of Delegates of the American Medical Association, through the Council on Medical Education and Hospitals and the Section on Pathology and Physiology, undertake an educational campaign to set forth these problems to the medical profession.

I suggest that this be referred to the Committee on Memorials and Communications.

SPEAKER FERNALD: I appoint the following for the Committee on Nominations: Deering G. Smith (chairman), Henry C. Sanders, Jr., Charles H. Parsons, Francis J. C. Dube, Earl J. Gage.

If there is no further business to come before the meeting, a motion is in order to adjourn.

DR. DYE: I move that we adjourn.

This motion was seconded and was carried.

Whereupon, the first meeting of the House of Delegates was adjourned at 10:45 p.m.

* * *

The House of Delegates convened at the Hotel Carpenter, Manchester, on Tuesday morning, May 14, at 8:30 with Speaker Fred Fernald, of Nottingham, presiding.

The following members answered the roll call:

The President, ex-officio
The Vice-President, ex-officio
The Secretary-Treasurer, ex-officio
Chester L. Smart, Laconia
Earl J. Gage, Laconia
Francis J. C. Dube, Center Ossipee
W. J. Paul Dye, Wolfeboro
Norris H. Robertson, Keene
Leander P. Beaudoin, Berlin
Lewis C. Aldrich, Jefferson
Leslie K. Sycamore, Hanover
John C. Eckels, Lisbon
Frederic P. Lord, Hanover
Deering G. Smith, Nashua
Henry O. Smith, Hudson
Clarence E. Dunbar, Manchester
George V. Fiske, Manchester
Clarence E. Butterfield, Concord
Warren H. Butterfield, Concord
Fred Fernald, Nottingham
Frederick S. Gray, Portsmouth
James Sanders, Rye
Edna Walck, Dover
Henry C. Sanders, Jr., Claremont

SPEAKER FERNALD: Has Dr. Smart a report to make?

DR. SMART: I have a report on the resolution that was read last night. There is a perfectly good reason why the pathologists should want such a resolution. One can understand that it is only fair, in many ways, that they should have it. But, some of the men, even last night, said that they were having a great many Wassermann tests done, for instance, which certainly would not be done if their patients had to pay for them. After all, that is a rather important thing, and if passing a resolution like this is going to cut down that type of diagnostic medicine, I think we should give it careful consideration before we recommend it.

DR. DUBE: Might I ask Dr. Burroughs to tell us what examinations are made in this State?

DR. TRAVIS P. BURROUGHS, Concord: We have three laboratory units of the State Board of Health; one is a chemistry unit at the State House; another is a bacteriology and serology unit at the State House; and the third is a bacteriology unit at Hanover.

We are not doing any tissue pathology. As I understand it, the laboratories of the Dartmouth Medical School have been doing tissue pathology for a number of years, but at least no tissue pathology is being done for or on behalf of the State Board of Health.

On the serological side, we are doing blood tests for syphilis, for undulant fever and for one or two other diseases, such as typhoid fever. On the bacteriological side, we are doing tests for communicable diseases. We are not doing any pregnancy tests.

One of the outstanding pieces of laboratory work that we have been doing in communicable diseases has been the typing of pneumococci. You will recall that two or three years ago, the House of Delegates called on the State Board of Health to start a pneumonia program, largely because of the reason that antipneumococcus serum was so costly that a great many people were not getting serum treatments, and because those who could pay for it were rather inclined to put off treatment until such a time as it was not effective.

It is unfortunate that antipneumococcus serum is effective for only one or two out of thirty-two possible types, and it is also unfortunate, in spite of what the detail men of the supply houses tell us, that it is a very difficult thing to type pneumococci accurately.

On account of the experiences they have had in Massachusetts and other places where pneumonia programs have been in progress quite a while, it was essential that the State should do the laboratory work on the basis of which it issued its serum, or else it should make a check against laboratory work which was reported to it, in connection with a request for specific serum. That is one of the points where the work of the laboratory has increased markedly.

The other thing that has increased under federal grants-in-aid has been the matter of the blood testing for syphilis. Blood testing is absolutely a part of the program for the detection of cases of syphilis, and, as you know, the detection of cases of syphilis and getting them under treatment are the only ways we have of cutting down the incidence and prevalence.

Another thing in connection with the blood testing for syphilis is that all the tests are difficult; so much so that the people who have been evaluating the efficiency of laboratories doing such tests have come to the conclusion that no laboratory should attempt to do them unless it is doing at least fifty specimens a week. I do not believe there are many laboratories in New Hampshire that have an opportunity to do fifty specimens a week. Hence, unless there is going to be a series of private laboratories established specifically for the purpose of testing syphilis, the State Laboratory is probably the most convenient place to send specimens.

Another part of the syphilis blood-testing program, which has expanded tremendously, has been in connection with the various things the State has required. As you know, the Legislature has required that every applicant for marriage

license shall have a Wassermann, Kahn, or some similar standard laboratory test for syphilis. It is specifically set forth in the law that that shall be done, without charge, by the State Board of Health. That was one of the reasons that the law was passed. I am quite sure if it had not been stated to the Legislature that those examinations would be made without charge to the applicant, there would have been enough votes to have prevented the law from passing.

We also have the matter of the annual blood testing of hairdressers, and the annual blood testing of barbers. Those are not matters of law, but of regulation.

I should like to bring up one other point here, because it has been a matter of discussion for a number of years. I refer to the distinction between the practice of medicine and the practice of laboratory technology. It is our intention, in the State Laboratory of Hygiene, not to practice medicine, and the laboratory people have specific instructions that they are not to make diagnoses.

You will recall that when the premarital blood-test law was put through, it was specifically stated that marriage should not depend on whether the Wassermann was reported positive or negative by the laboratory, but should depend on whether the physician, certifying as to the applicant, said that the applicant should or should not be permitted to marry.

I feel that the answer is this. The laboratory should stick to laboratory work, and leave the diagnosis and treatment to the physician. I do not believe that, under those circumstances, it is necessary, from a technical point of view, to have the laboratory work done by a physician.

SECRETARY METCALF: I move that this matter be laid on the table.

This motion was seconded and was carried.

DR. SYCAMORE: Every year, there comes before the House of Delegates a number of questions of policy which are quite important. Frequently, these questions have a lot of implications; the average delegate does not have a chance, in the time the questions are before the House, to consider the implications and to make any decision of his own.

I move that the chairman of the Committee on Officers' Reports and the chairman of the Committee on Memorials and Communications each be instructed to submit to the Secretary, not later than two weeks before the annual meeting, a statement of any questions of policy which will be brought before the House of Delegates in the report of their committees, and I further move that the Secretary be instructed to add to these lists a statement of any similar questions of which he has knowledge and transmit the complete list to each member of the House of Delegates in advance of the annual meeting.

The motion was seconded and was carried.

DR. SANDERS: I wish to bring up for reconsideration the motion that the round-table conferences be continued.

It has come to my knowledge that there are a number of members of the Society who do not especially like these round-table discussions, and they would have, preferably, the old type of meeting, with papers. I move the reconsideration of the vote taken last night.

This motion was seconded and was carried.

DR. DYE: Inasmuch as the motion to reconsider has been carried, I should like to make a motion that each member of the Society be polled, with a return postal card.

This motion was seconded and was carried.

SPEAKER FERNALD: Is there any further business to come before this meeting?

If not, a motion is in order to adjourn.

DR. DYE: I move that we adjourn.

This motion was seconded and was carried.

Whereupon, the second meeting of the House of Delegates was adjourned at 9:30 a.m.

* * *

The House of Delegates convened at the Hotel Carpenter, Manchester, on Wednesday morning, May 15, at 8:30, with Speaker Fred Fernald, of Nottingham, presiding.

The following members answered the roll call:

The President, ex-officio
The Secretary-Treasurer, ex-officio
Chester L. Smart, Laconia
Earl J. Gage, Laconia
Leander P. Beaudoin, Berlin
Lewis C. Aldrich, Jefferson
Leslie K. Sycamore, Hanover
John C. Eckels, Lisbon
Frederic P. Lord, Hanover
Deering G. Smith, Nashua
Henry O. Smith, Hudson
Clarence E. Dunbar, Manchester
George V. Fiske, Manchester
Clarence E. Butterfield, Concord
Warren H. Butterfield, Concord
Fred Fernald, Nottingham
Frederick S. Gray, Portsmouth
James Sanders, Rye
Edna Walck, Dover
Henry C. Sanders, Jr., Claremont

SPEAKER FERNALD: Our first order of business this morning is the report of the Committee on Nominations.

Report of the Committee on Nominations

OFFICERS

President: Ezra A. Jones, John Z. Shedd, Richard E. Wilder.

Vice-President: Charles H. Dolloff, John A. Hunter, Henry C. Sanders, Jr.

Councilor for Merrimack County (five years: Henry H. Amsden.

Councilor for Hillsborough County (five years): Clarence O. Coburn.

Trustee (three years): Frederic P. Lord.

Speaker of the House of Delegates: Robert O. Blood.

Vice-Speaker of the House of Delegates: Timothy F. Rock.

Necrologist: Henry H. Amsden.

Delegate (American Medical Association, 1941-42): Deering G. Smith.

Alternate Delegate (American Medical Association, 1941-42): Emery M. Fitch.

Delegates (New England state medical societies, 1940): as printed in program.

STANDING COMMITTEES

Amendments to Constitution and By-Laws: James B. Woodman, Chester L. Smart, Frederick S. Gray.

Control of Cancer: George C. Wilkins, Howard N. Kingsford, George F. Dwinell.

Medical Economics (three years): Leslie K. Sycamore.

Medical Education and Hospitals (three years): John P. Bowler.

Mental and Social Hygiene: Charles H. Dolloff, Benjamin W. Baker, John B. McKenna.

Publication: Carleton R. Metcalf, Warren H. Butterfield, Ellsworth M. Tracy.

Public Relations: The President, the Vice-President, the Secretary-Treasurer, Robert J. Graves, Joseph N. Friborg.

Scientific Work: Carleton R. Metcalf, Frederick P. Scribner, Nathan T. Milliken.

Tuberculosis: Robert B. Kerr, Robert M. Deming, M. Dawson Tyson.

SPECIAL COMMITTEES

Child Health: Colin C. Stewart, Jr., Travis P. Burroughs, Franklin N. Rogers.

Maternity and Infancy: Robert O. Blood, Benjamin P. Burpee, Marion Fairfield.

Medical Relief: Robert J. Graves, John P. Bowler, Roland J. Joyce.

DEERING G. SMITH,
HENRY C. SANDERS, JR.,
CHARLES H. PARSONS,
FRANCIS J. C. DUBE,
EARL J. GAGE.

SPEAKER FERNALD: The next order of business is voting, by ballot, for president. I appoint the following as tellers to collect and count the votes: Clarence E. Dunbar and Frederick S. Gray.

The ballots were cast and counted.

DR. DUNBAR: Eighteen votes were cast for Ezra A. Jones.

SPEAKER FERNALD: Ezra A. Jones is elected president for next year.

The next order of business is the election of the vice-president by ballot.

The ballots were cast and counted.

DR. DUNBAR: There were eighteen votes cast; one for Dr. Hunter, five for Dr. Sanders and twelve for Dr. Dolloff.

SPEAKER FERNALD: Charles H. Dolloff is elected vice-president for next year.

DR. LORD: I move that the Secretary cast one ballot for the rest of the nominations submitted by the Committee on Nominations.

This motion was seconded and was carried.

SECRETARY METCALF: The Secretary has cast the ballot.

SPEAKER FERNALD: I declare the rest of the slate, as submitted by the Committee on Nominations, duly elected.

DR. WILKINS: In 1932, when I was president of the Society, there was a change in the by-laws which created the Benevolence Fund. At that time, the original amendment provided for $1 a year being taken from the dues of each member to be applied to the Fund. The amendment was changed by the House of Delegates to 50 cents. That means that during these years, there has been approximately $250 paid in each year for this fund. Now at the end of eight years it has reached only the sum of $2300.

It was too late yesterday to offer an amendment to increase the amount to $1 to be added each year, but that will be brought in next year. Dr. H. O. Smith has suggested that it would be possible to take $1000 from the General Fund, and transfer it, if the House of Delegates is willing.

My motion is that the Trustees be instructed to transfer at least $1000 from the General Fund to the Benevolence Fund.

This motion was seconded and was carried.

SECRETARY METCALF: Gentlemen, I move that we express our gratitude to the Manchester group of doctors for the work they have done this year, and I suggest, if they are willing, that they take up the burden again for 1941.

This motion was seconded and was carried.

SECRETARY METCALF: I move, also, that we express our thanks for the work that Dr. Harris E. Powers has done, and the large amount of time that he has given to the Society for this meeting.

This motion was seconded and was carried.

SPEAKER FERNALD: If there is no further business, a motion is in order to adjourn.

DR. COBURN: I move that we adjourn.

This motion was seconded and was carried.

Whereupon, the 1940 meeting of the House of Delegates was adjourned at 9:20 a.m.

REPORT ON MEDICAL PROGRESS

THE TREATMENT OF THE ARTHRITIDES OF KNOWN ORIGIN*

WALTER BAUER, M.D.,† AND CHARLES L. SHORT, M.D.‡

BOSTON

LAST year's progress report[1] having been devoted to the classification and diagnosis of the various arthritides, it seems appropriate that the one for this year should deal with the treatment of joint diseases of known etiology. The management of articular disorders of unknown cause will be discussed in a subsequent report.

The physician must ever be aware that accurate diagnosis is a prerequisite for the successful treatment of articular diseases. His diagnostic skill is greatly enhanced if he follows a useful classification of articular diseases.

TRAUMATIC ARTHRITIS

Under traumatic arthritis is included strain, sprain, intra-articular derangements, traumatic synovitis and fracture into the joint. We must not forget that trauma may determine the localization of either specific infectious or rheumatoid arthritis, initiate an acute phase of degenerative joint disease or precipitate an acute attack of gouty arthritis.

The treatment of an acute traumatic arthritis depends on its location as well as on the type and severity of the injury sustained. Restoration of the anatomic relation of the articular and periarticular structures by conservative or operative treatment is most important. Following this, immobilization and complete physiologic rest by means of adhesive strapping, splints, plaster casts or other suitable apparatus are indicated. The joint should be kept at complete rest until muscle spasm and effusion have disappeared. Normal joint motion and muscle strength are finally restored with the aid of carefully supervised physiotherapy.

The application of heat or cold may relieve discomfort. Painful effusions should be aspirated. In such cases examination of the synovial fluid is of diagnostic value. An acute traumatic effusion rarely contains more than 1000 leukocytes per cubic millimeter, with polymorphonuclears ranging from 0 to 20 per cent. Erythrocytes are frequently observed. In some cases frank intra-articular hemorrhage will be detected. Following aspiration, a compression bandage should be applied.

For more detailed instructions pertaining to the treatment of acute joint injuries, one should consult a surgical or orthopedic textbook. Failure to institute adequate therapy of the type outlined may result in chronic joint disability, characterized by pain, chronic effusion, loss of normal joint function, muscle atrophy and finally post-traumatic monoarticular degenerative joint disease.

SPECIFIC INFECTIOUS ARTHRITIDES

The advent of sulfanilamide has established beyond all doubt that effective chemotherapy against microbial disease is possible. The introduction of sulfanilamide and allied compounds in the treatment of many of the specific infectious arthritides

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From the Medical Clinic, Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.

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represents the greatest advance ever made in the treatment of joint disease. With specific therapy available for many of these arthritides, there should be less need for surgical drainage, better end results, fewer days of illness and less economic loss. Since orally administered, relatively inexpensive compounds have proved most effective in the treatment of the specific infectious arthritides, all physicians should be thoroughly acquainted with the practical aspects of their administration. Contraindication to their use, dosage, toxic reactions and the types of joint disease in which they are indicated will be taken up as the treatment of each form of specific infectious arthritis is discussed.

Tuberculous Arthritis

There is no specific treatment for tuberculous arthritis. Because tuberculosis of the joints is only one manifestation of a tuberculous infection, all authorities are agreed that rest for both the local lesion and the patient should be the keystone of all therapy. Good food, fresh air and hygienic surroundings are essential. Heliotherapy is a valuable adjunct in the treatment of tuberculous joints, but convincing proof is lacking that it alone is sufficient.

It has long been known that bony ankylosis results in the cure of a tuberculous joint, and this has been considered by many to be the most desirable end result. Unfortunately, it rarely occurs in the natural course of the disease. Surgical fusion of tuberculous joints with resulting bony ankylosis has gradually been accepted as the approved method of treatment, despite the fact that it met with widespread opposition at the time of its introduction. Some workers have contended that immobilization of an affected joint by means of a brace, plaster cast or other type of apparatus gives end results fully as good as those achieved through operative interference. The time required for cure by the latter method is longer and complete arrest of the disease process is less certain. The question of operative interference must always be decided on the merits of the individual case. In one case, arthrodesis might be beneficial; in another, the operation might be dangerous or useless. The reader who is interested in a more detailed discussion of the treatment of tuberculous arthritis should consult authoritative treatises.[2-4]

Gonococcal Arthritis

The specific value of any therapeutic measure can be established only if one is able to demonstrate that the clinical course of the disease is strikingly altered by it in a large percentage of cases. The results with sulfanilamide therapy indicate clearly that this drug is specific for gonorrhea and its complications. It has proved as efficacious as its much-heralded predecessor, fever therapy. Its advantages over fever therapy are many.[5, 6] Administration is much less complicated and does not require a special apparatus or a trained personnel. It is a less heroic and less dangerous form of therapy. The primary focus is more frequently cured with sulfanilamide therapy than it is with hyperpyrexia. Most important of all, it is relatively inexpensive and is therefore available for the treatment of all types of gonorrhea.

General treatment. A patient with gonococcal arthritis should be kept at rest in bed if a weight-bearing joint is involved, or if either fever or sulfanilamide therapy is administered. The diet is not important; it should be well balanced and suited to a patient with an infectious disease. The fluid intake is regulated in accord with the type of therapy employed; fluids are forced in the patient receiving no specific therapy or hyperpyrexia and are restricted when sulfanilamide is given. An acutely inflamed joint may require complete rest in a splint or cast. Pain due to marked intra-articular distention may be relieved by aspiration. Analgesics or opiates may be necessary until relief is obtained from specific therapy.

Sulfanilamide and sulfapyridine therapy. The only absolute contraindication to the administration of sulfanilamide is a known hypersensitivity to the drug,[7] but liver disease, blood dyscrasias and renal disease usually contraindicate its use.[8]

The dose of sulfanilamide administered and the regularity with which it is given are extremely important if one is to obtain the largest possible percentage of cures. Many of the reported failures have resulted from improperly administered or inadequate doses of the drug or from failure to keep the fluid intake constant. *In treating patients with sulfanilamide, the desired blood level must be maintained. This can be achieved only by administration of the drug every four hours, day and night, and by maintenance of a constant fluid intake.* The observance of this simple rule is imperative because sulfanilamide is as readily excreted by the kidneys as it is absorbed by the gastrointestinal tract.[8, 9] A total twenty-four-hour fluid intake of 1500 to 2000 cc. is adequate for most patients with gonococcal arthritis receiving sulfanilamide. Maintenance of a constant fluid intake, provided it is not excessive, is more important than the amount allowed for any twenty-four-hour period. An excessive intake results in an increased urinary output, which in turn reduces the blood sulfanilamide to a lower level than that expected from the dose given. If an excessive

intake is allowed, a larger dose of the drug will be required to maintain the desired concentration of sulfanilamide in the blood.

We advocate large doses of sulfanilamide in the treatment of gonococcal arthritis, believing that this mode of administration ensures the highest percentage of cures.[5, 10] *The dose is calculated in the following manner: 0.05 gm. (¾ gr.) per pound of body weight, provided the total dose does not exceed 8 gm.* The calculated dose represents the amount to be given each day following the initial twenty-four-hour amount.

The dose having been calculated, the drug is administered orally in one of two ways. One half the calculated dose is given initially and again in four hours, then one sixth the calculated dose is administered every four hours, day and night; or one sixth the calculated dose is given initially and every four hours. When the drug is given according to the first schedule, a blood sulfanilamide level of from 10 to 15 mg. per 100 cc. or higher results, whereas the second schedule allows for the maintenance of a blood sulfanilamide level of between 5 and 10 mg. per 100 cc.

Although sulfanilamide cures are experienced when the blood sulfanilamide level remains as low as 3 to 5 mg. per 100 cc. throughout the period of therapy, it has been our experience that more cures are obtained when the level is maintained at 10 mg. or higher. This is extremely important in such a serious gonococcal complication as arthritis, which may go on to joint destruction.

The exact length of time the drug should be administered depends largely on the patient's response. In mild cases where the joint symptoms clear rapidly and gonococci can no longer be demonstrated by culture or smear in the genitourinary focus, the dosage may be reduced by one third or one half in the second week. In severe cases full dosage had better be continued for at least two weeks. In most cases of gonococcal arthritis, marked improvement is noted within forty-eight to seventy-two hours. If such improvement is not observed, the dose of the drug should be increased, if necessary until a blood sulfanilamide level of 20 mg. per 100 cc. has been obtained. If the arthritis shows no apparent response to sulfanilamide therapy once such blood levels have been obtained, the diagnosis should be carefully checked. There is always the possibility that such failures result from sulfanilamide-resistant gonococcal strains or failure of some inherent host factor to play its usual role. Those patients who fail to respond to large doses of sulfanilamide can subsequently be treated with sulfapyridine or fever therapy. Our present rule is to try sulfapyridine. Sulfapyridine should be administered as follows: 2 gm. initially and in four hours, then 1 gm. every four hours during the first twenty-four hours, then 1 gm. every four or six hours, day and night. This dosage should be continued for at least one full week. If improvement results, the dose can be reduced by one third or one half during the second week. The clinical reports to date have not shown that sulfapyridine is superior to sulfanilamide in the treatment of gonococcal arthritis, provided the latter drug is given in adequate doses. Uleron (sulfanilyl dimethyl sulfanilamide) is not so effective and may produce peripheral neuritis.

Parenteral administration of sulfanilamide is very rarely indicated in acute gonococcal arthritis, except in the rare case complicated by pelvic peritonitis or meningitis, because the drug is usually well tolerated by mouth. This is most fortunate, because it is practically impossible to maintain a constant blood sulfanilamide level when the drug is administered parenterally.

Because of the regularly occurring acidosis encountered in sulfanilamide therapy, certain workers[7, 11] have advocated the administration of regular doses of sodium bicarbonate in amounts up to 3.6 gm. per day. The routine administration of sodium bicarbonate in the doses advocated would not begin to compensate for the alkali loss resulting from sulfanilamide therapy.[12] Its administration is optional and not imperative. In some cases it does seem to reduce somewhat the associated nausea and vomiting.

Sulfanilamide can be safely administered only if the patient is under careful clinical and laboratory observation. The red-blood-cell count and white-blood-cell count should be determined at least every three days. The patient should be carefully observed for the development of toxic symptoms, which have been very adequately described by various workers.[7, 13, 14]

The milder toxic symptoms do not indicate serious complications. Many of them represent the symptoms of acidosis. If the acidosis is marked, it can be relieved by large oral doses of sodium bicarbonate or racemic sodium lactate. When the acidosis requires parenteral therapy, a 1/6 M (molar) solution of racemic sodium lactate is the medication of choice. Varying grades of cyanosis are seen in all patients receiving large doses of sulfanilamide. It is not an alarming symptom and can usually be disregarded.

Fever develops in 10 to 15 per cent of patients.[14] It usually occurs during the first week of sulfanilamide administration. Omission of the drug results in its subsidence within thirty-six to forty-eight hours, thus proving that sulfanilamide and

not gonococcal arthritis or some other complication is responsible for the increased temperature. Since fever may be the first sign of severe hemolytic anemia, granulocytopenia, hepatitis or a skin eruption, it is obvious that fever constitutes the most important warning signal. In the absence of these complications, readministration of the drug may be tried in severe cases.

A severe hemolytic anemia may occur during the first week of treatment,[13] necessitating the immediate withdrawal of the drug and the use of transfusions. In many patients no alteration of the red-cell count is observed. Approximately one third of the patients develop a moderate anemia of a subclinical hemolytic nature,[5] accompanied by a reticulocytosis, and when the drug is discontinued a spontaneous gradual rise of the red cells and hemoglobin to the pre-treatment level occurs. Transfusions are rarely required, and the drug need not be stopped unless the red-cell count falls below 3,000,000.[5] Provided the patient has been on a good diet, the use of liver or iron has not been shown to increase the speed of recovery. If the patient is already anemic before treatment is started, transfusions should be given before or with the administration of the drug.[5] In every case, the red-cell count should be done at three-day intervals during treatment.

Leukopenia and agranulocytosis may develop during sulfanilamide treatment,[5, 15–17] usually about the second week. If agranulocytosis develops the drug should be omitted and fluids forced, and transfusions may be necessary.

Skin rashes may result from administration of sulfanilamide and are associated with fever.[7, 13] Both usually disappear promptly on discontinuance of the drug. In certain cases erythema and edema may result from exposure to sunlight. For this reason patients receiving sulfanilamide should not be exposed to sunlight or ultraviolet radiation. Any skin complication is a contraindication to further sulfanilamide administration.

The occurrence of hepatitis as a toxic manifestation of sulfanilamide therapy has been reported,[7] and in some cases has terminated fatally. If this complication should arise, the drug should be discontinued, fluids forced and a high-carbohydrate intake prescribed.

The symptoms of sulfapyridine toxicity are the same as those of sulfanilamide, with the addition of the appearance of sulfapyridine crystals in the urine, hematuria, gross or microscopic, and anuria. The latter complications occur more frequently if the fluid intake is less than 2000 cc. per day. Patients receiving sulfapyridine should have a urine examination every second day in addition to red-cell and white-cell counts.

Fever therapy. Although the introduction of fever therapy marked a great advance in the treatment of gonococcal arthritis, it has fallen into discard because of the almost uniform response of such cases to sulfonamide compounds. Its use is still indicated in the occasional patient in whom the use of sulfanilamide and sulfapyridine is contraindicated or in whom sulfonamide compounds have failed. When employed it should be administered by a trained hospital personnel.[18] If this is impossible, artificial fever may be induced by typhoid vaccine intravenously.[19] In such cases the fever can usually be maintained by the use of hot-water bottles and blankets.

Manipulative measures aimed at treating the primary focus during the acute phase should be omitted if possible in order to avoid a recurrent bacteremia and further extension of the arthritis although this danger is materially reduced if they are undertaken while sulfanilamide is being administered. There is no contraindication to combining the more simple procedures, such as irrigation and douches, with sulfanilamide therapy. That gonococcal vaccines and filtrates are efficacious in the treatment of gonococcal infections has never been proved. We do not employ them.

Once the joint has become painless and the inflammation has largely disappeared, active motion is desirable in order to hasten the return of normal function. This can be accomplished by adequate physiotherapeutic measures and protection against unusual or faulty weight-bearing. In patients in whom treatment was instituted too late to prevent permanent joint damage, more formidable orthopedic measures such as arthroplasty or arthrodesis may be necessary.

Septic Arthritis

Although invasion of the articular cavity by any organism may result in a septic arthritis, staphylococci, hemolytic streptococci and colon bacilli are the commonest offenders. Such bacteria may reach the joint via the blood stream, by direct extension from a neighboring focus or by way of a penetrating wound. The earlier the diagnosis is made, the better will be the therapeutic results. Early diagnosis must depend on aspiration and bacteriological examination of the fluid.

General treatment should be instituted early and should consist of immobilization of the joint, repeated joint aspirations, analgesics or opiates if required, maintenance of a good dietary intake and a positive fluid balance, and transfusions if indicated. Once the bacteriological diagnosis has been established, chemotherapy should be instituted. In the case of infection due to either the hemolytic streptococcus or the colon bacillus, sulfanilamide should

be used in the same dosage outlined under gonococcal arthritis. If improvement is not experienced within seventy-two hours, the dose should be increased, or sulfapyridine should be administered in full doses. The general condition of the patient, the appearance of the joint and the results of the analyses of the repeated synovial fluid aspirations will enable one to determine whether surgical drainage is required. The results to date indicate that there will be less need for surgical interference in the future than there has been in the past.

Sulfathiazole is probably the most effective chemotherapeutic agent at our disposal for the treatment of staphylococcal arthritis, although sulfapyridine has been reported to be effective in staphylococcal septicemia. Sulfathiazole should be administered in 1-gm. doses every four hours, day and night. Once obvious improvement has been observed, the dose can be reduced to one half the amount. If the staphylococcal infection is not amenable to sulfathiazole therapy, free dependent drainage with the continuation of chemotherapy offers the best chance for a normal, movable joint.

Joint ankylosis due to septic arthritis may be treated by arthroplasty after it has been quiescent for several years.

Pneumococcal Arthritis

Pneumococcal arthritis is encountered as a complication of pneumococcus pneumonia in approximately 0.1 per cent of cases. The primary form is rare. Bacteriological examination of the aspirated synovial fluid is necessary for diagnosis. It should not be confused with the arthritis of serum sickness following the administration of antipneumococcus serum. In addition to good medical care, treatment consists of early immobilization, repeated aspirations and the administration of full doses of sulfapyridine. Chemotherapy will probably obviate surgical drainage, which was so often necessary in the past.

Typhoidal Arthritis

Typhoidal arthritis is a rare complication of typhoid fever. Suppuration and ankylosis of the involved joints rarely occur. The presence of typhoid fever, or a history of a recent typhoidal infection, with the recovery of organisms from the involved joints, establishes the diagnosis. This type of arthritis is seldom encountered because of the decreasing incidence of the disease. Fixation of the joint and repeated aspirations are probably the only forms of therapy indicated in most cases. The treatment of the spinal form of typhoidal arthritis consists in fixation of the spine with a plaster shell or brace until the process becomes quiescent. Rarely is surgical interference necessary or indicated.

Meningococcal Arthritis

In severe meningococcal infections, usually accompanied by a hemorrhagic rash, multiple joints may become painful and tender, without associated marked swelling or effusion. Such joint symptoms are thought to be due to hemorrhages into the articular and periarticular tissues. They are transitory in nature, and their treatment is symptomatic.

The metastatic pyoarthrosis is a complication of meningococcal infection which usually appears at the end of the first week. It is usually monoarticular. Aspiration of the joint reveals the presence of meningococci in the synovial fluid. Treatment of this type of meningococcal arthritis consists of fixation, repeated aspirations and the use of sulfanilamide in adequate dosage. Rarely if ever is surgery indicated.

Chronic meningococcal septicemia often presents itself as a case of unexplained fever, with associated recurrent embolic rashes and intermittent migratory arthritis. Treatment should be directed toward the eradication of the systemic meningococcal infection, the joints being of secondary importance. Here again, sulfanilamide administration in adequate dosage is indicated.

Syphilitic Arthritis

The articular manifestations of congenital syphilis are known as Clutton's joints, or tenosynovitis syphilitica. The disease is self-limited and usually not influenced by treatment. Since the ultimate prognosis is good, whether treated or not, the importance of diagnosis lies first in the recognition of syphilis in the patient and his family, and secondly in distinguishing this form of joint disease from tuberculous or rheumatoid arthritis.

That an acute form of arthritis may be a manifestation of secondary syphilis has been proved by the demonstration of spirochetes in synovial fluid by rabbit inoculation. The diagnosis is rarely difficult. If rapid improvement does not ensue following the institution of antisyphilitic treatment, one should suspect that the patient is probably suffering coincidentally from some other form of arthritis.

Tertiary syphilis may involve any one of the joint structures. In rare cases biopsies may be necessary in order to distinguish tertiary syphilis from neoplastic disease of the bone. If the patient shows evidence of syphilis elsewhere or a positive Wassermann reaction, a trial of antisyphilitic therapy is indicated. If the existing lesion does not respond to such treatment, the diagnosis should be questioned.

Charcot joints secondary to tabes dorsalis will be covered in the section devoted to neuroarthropathies.

Arthritides Associated with Other Infectious Diseases

Brucellosis may be accompanied by arthritis, the treatment of which should be aimed at the eradication of the systemic infection. Rarely, a suppurative arthritis secondary to an osteomyelitis is encountered. When present, it requires surgical drainage.

Arthritides associated with bacillary dysentery, Haverhill fever, Reiter's disease and the exanthemas, exclusive of scarlet fever, rarely if ever represent a serious complication. The treatment is symptomatic, consisting of analgesics, temporary fixation of the joint if necessary and aspiration for relief of pain due to articular distention.

The rare cases of arthritis in association with subacute bacterial endocarditis (*Streptococcus viridans*) are the results of septic emboli lodging in or around the joints. The inflammation usually disappears in a matter of days, suppuration does not take place, and specific measures are never necessary.

The joint manifestations of scarlet fever are of three distinct types. The acute type of polyarthritis represents the onset or reactivation of rheumatic fever. Its treatment is the same as that for rheumatic fever. The nonsuppurative type of arthritis, with sterile effusion, usually occurs during the first two weeks of the disease and is frequently migratory in character. It does not require specific therapy. The patient is made more comfortable by the judicious use of analgesics, heat and, occasionally, splinting. Septic arthritis due to the actual invasion of the articular structures by the hemolytic streptococcus sometimes occurs, usually in the second or third week of the disease. The treatment is the same as that outlined under septic arthritis.

Arthritis may be a manifestation of lymphogranuloma venereum. Because the arthritis is self-limited, evaluation of therapy is extremely difficult. Some success has apparently been obtained with sulfanilamide when administered in adequate dosage.[20]

Neuropathic Arthritis (Charcot Joints)

Neuropathic joints are most commonly associated with tabes dorsalis, syringomyelia and leprosy, and rarely with injuries or with other diseases of the spinal cord and peripheral nerves. Whatever the origin, the management is the same. Antisyphilitic medication is without effect in arresting the neuropathic arthritis associated with tabes dorsalis. The treatment of the neuroarthropathies is for the most part an orthopedic problem, and includes the use of braces and other forms of apparatus. When weight-bearing or spinal joints are involved, early fusion is the method of choice and offers the best chance of arresting the disease process. In syphilitic neuroarthropathy, antisyphilitic therapy should be administered before and after surgical interference. If any form of apparatus is used, it should be well padded in order to prevent pressure sores.

Gouty Arthritis

The history alone should suggest the correct diagnosis in the majority of patients suffering from gouty arthritis. It is generally agreed[21–23] that the uric acid concentration of the serum is increased in this type of arthritis and that the pathologic changes observed are the result of the deposition of monosodium urate.[23] Although there is considerable evidence favoring the view that gout is a metabolic disease, its exact nature is unknown. Recurrent attacks of acute arthritis with complete freedom from joint symptoms in the intervals are characteristic of the disease. The time between the first and second attacks is variable. It may be months or years, the average time being eighteen months. The interval between attacks tends to decrease with each subsequent attack until chronic joint deformity becomes evident. The treatment of patients with gouty arthritis raises many questions: How should one treat the acute attacks? What treatment should be prescribed during the intervals of freedom? Can chronic gouty arthritis be prevented, and if not, how should it be treated? Does therapy influence the hyperuricemia? Are acute attacks preventable? Can one materially alter the course of the disease? Should one restrict the intake of purine, and if so, to what extent and when?

The proper treatment of acute gouty arthritis is very gratifying to both patient and physician. Colchicine, if correctly administered, is practically a specific form of therapy for the acute attacks. We have never seen it fail to give relief. It should always be given in the crystalline form, because the potency of the wine or tincture of colchicine is extremely variable. We prescribe 1/120 gr. every one or two hours until relief from pain is obtained or until diarrhea, nausea, or vomiting appears. From eight to sixteen doses usually suffice, but occasionally more are necessary. The drug is then discontinued. Freedom from pain and subsidence of swelling occur within twenty-four to seventy-two hours. The diarrhea is usually sufficiently severe to require treatment with

paregoric; 4 cc. is given for each loose bowel movement until the diarrhea is checked. Once the patient has established the amount necessary to produce such symptoms, he can reduce the total dose by one or two pills or granules and still obtain the desired effect without experiencing severe gastrointestinal symptoms. We have never observed any other untoward effects. Hypersensitivity to the drug is unknown, nor does it lose its efficacy with repeated administration. The patient should always carry colchicine with him. The appearance of any of the usual prodromes[22-24] calls for immediate institution of colchicine therapy. If the patient always follows these rules, many prolonged and incapacitating attacks may be prevented.

Absolute bed rest is always indicated during the attacks, particularly when weight-bearing joints are involved. Avoidance of even normal joint use prevents recurrent minor traumas and thereby shortens the attack. Premature resumption of normal activity may precipitate another attack. Occasionally opiates are necessary until the full effect of the colchicine has been obtained. Hot compresses or packs every three hours may be helpful. Moist heat is always preferable to dry. An occasional patient insists that cold gives more relief than any form of heat. We never employ cinchophen because of the attendant risks and the fact that the colchicine when administered properly is more efficacious. The only other measures we employ for acute gouty arthritis are an increased fluid intake and the avoidance of the few foods with a high purine content. No one has ever proved that an acute attack is materially shortened by a diet free of or low in purine content.[23]

Certain workers[24] contend, without presenting the necessary proof, that adherence to a rigorous regime during the symptomless periods will reduce the number of subsequent attacks and sufficiently alter the course of the disease to prevent chronic gouty arthritis. We cannot agree with such claims. Evaluation of the effect of therapy on the course of a disease as variable from patient to patient as is gout is extremely difficult. Those who think the course of gout can be altered believe that carbohydrates and proteins promote urate excretion and that fat inhibits it, and therefore prescribe a diet low in purine (100 to 150 mg. as compared with the normal intake of 600 to 1000 mg.) and fat, high in carbohydrate and protein. A high-protein, low-purine diet of this type is possible if one gives generously of such protein foods as milk, cheese and eggs. Until proof is forthcoming that this type of dietary favorably influences the hyperuricemia and the clinical course of gout, its prescription is hardly justified. It is a monotonous diet to which few people will adhere. In addition, it favors a deficiency of certain proteins, iron and vitamin B. We prescribe a diet of moderate purine content. This is readily accomplished by omitting with some regularity the few foods with a high purine content.* Absolute restriction of alcohol is frequently advocated without adequate proof that such abstinence is therapeutically beneficial. If small amounts of alcohol are allowed, whisky is probably preferable.

Some writers[24] believe that cinchophen in 7½-gr. doses three or four times a day, three or four days out of each week, will aid in controlling the symptoms and hyperuricemia of gout. Such therapy may be symptomatically effective but does not reduce the hyperuricemia, and it may be harmful.[23] Furthermore, sodium salicylate in doses of 60 to 100 gr. a day, three or four days out of each week, will result in an equally great urate diuresis as that which occurs with cinchophen. Therefore, we prefer the repeated administration of salicylates. Thiamin chloride and glycine administration are not beneficial.

A fluid intake of 3000 to 4000 cc. a day should be encouraged in order to maintain a high urinary output. The latter may allow for an increased urinary urate excretion and will protect the kidney against uric acid stone formation. However, this is best accomplished by keeping the urine alkaline through the administration of three or four teaspoonfuls of sodium citrate each day. The patient himself can make a reasonably accurate urine pH determination by using nitrazine paper.

The gouty patient should be warned that trauma, major or minor, physical or physiologic, and other provocative factors may precipitate an acute attack of gouty arthritis.[23, 24] Major operative procedures may do the same.[24]

Chronic gouty arthritis and its complications are difficult to treat. Colchicine, 1/120 gr. three times a day, may be helpful. Regular rations of salicylates are often necessary. Orthopedic measures, including physiotherapeutic procedures, joint aspirations, immobilization, correction of deformities by casts or operative interference and so forth may be indicated. Troublesome tophi can be excised with safety. Excellent foot care should always be provided.

Hemophilic Arthritis

Arthritis is one of the commonest manifestations of hemophilia. It may present itself in one of two forms: acute hemarthrosis, the result of a single intra-articular hemorrhage, and the chronic

*These include anchovies, beef, brain, gravies, kidneys, liver, meat extracts, sardines and sweetbreads.

form, which is usually the result of repeated intra-articular bleeding. Permanent reduction of the increased clotting time is the only type of treatment that would prevent and control hemophilic arthritis. To date, no such therapy is known. Treatment of the acute hemarthrosis should consist of rest and immobilization with a splint or plaster cast until the bleeding stops and the acute inflammation has subsided. If the pain caused by the sudden intra-articular distention is severe, cautious aspiration with a small-bore needle may be undertaken, but under no circumstances should aspiration be performed until the clotting time has been reduced by means of transfusion. This method of treatment allows for a more rapid subsidence of the signs and symptoms. During the stage of recovery, mild, active exercise and massage are permitted. In the chronic form, correction of deformities may be accomplished by slow traction or other gradual and gentle methods of improving position and gaining motion. Walking calipers and braces may be helpful if weight-bearing joints are involved. Under no circumstances should the joints be strenuously manipulated or opened.

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Anaphylactic Arthritis

The arthritis of serum sickness is the only type of arthritis that can be classified as anaphylactic or allergic in nature. Its recognition is never difficult. It is a self-limited disease which clears completely, leaving no residual signs. The treatment of this type of arthritis is entirely symptomatic. Analgesics, usually one of the salicylates, are indicated. Heat is often helpful. Hypnotics are occasionally required. Epinephrine, if helpful at all, should be used at the onset of the complication. Further trial of the use of histaminase in both the prevention and treatment of serum sickness is necessary before concluding that it is of value for this type of arthritis.

Arthritis as a Manifestation of Other Diseases

There is no known specific therapy for the articular manifestations of erythema nodosum, acute disseminated lupus erythematosus, purpura and pulmonary osteoarthropathy. In some cases symptomatic measures such as heat, analgesics, opiates and splinting are necessary and beneficial.

The term "psychosomatic rheumatism" is employed to designate the ill-defined skeletal aches and pains experienced by the psychoneurotic individual. Psychotherapy is indicated in such cases, but a definite statement of its results must await further study.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26341

PRESENTATION OF CASE

A sixty-year-old American taxicab driver was admitted to the hospital complaining of severe headaches.

The patient was in his usual vigorous health until six months before entry when he was stricken, while driving his cab, with a headache which became increasingly severe, necessitating his going home. The headache was located over the left eye and in the region of the occiput, whence it radiated down the neck. It persisted almost continuously until the time of admission. He noted that coughing, stooping and straining at stool aggravated the pain, which was only temporarily relieved with medicaments prescribed by two or three local physicians. Four months before entry occasional diplopia with blurring and dimness of vision had occurred, and had persisted intermittently. He stopped work three months before entry in an unsuccessful attempt to obtain relief from his symptoms by rest. During the month before admission he vomited precipitously three or four times after eating; he noted frequent faint spells, and ten days before entry he fell, struck his head and was unconscious for a few minutes. He had lost 25 pounds in weight during his illness, had experienced an impairment in memory and, at times, had noted dyspnea and orthopnea, with nocturia two to three times.

The marital and family histories were essentially negative. He had had scarlet fever at the age of twelve, without known complications.

Physical examination revealed a well-developed and well-nourished but drowsy and mentally clouded man complaining of severe headache. The fundi showed cotton-wool exudates with flame-shaped perimacular hemorrhages, especially on the left. The external ocular movements were normal. The ears, nose, mouth and throat were essentially normal. The apex of the heart was percussed at the midclavicular line in the fifth interspace; the sounds were loud, the rhythm regular, and the aortic second sound loud and snapping. The blood pressure was 195 systolic, 140 diastolic. The lungs were normal. The abdominal, rectal and neurological examinations were negative.

The temperature, pulse and respirations were normal.

The blood showed a red-cell count of 5,200,000 with 72 per cent hemoglobin (Sahli), and a white-cell count of 12,000 (later 18,000) with 80 per cent polymorphonuclears. A lumbar puncture showed normal dynamics. The spinal fluid had a total protein of 216 mg. and a sugar of 62 mg. per 100 cc. A blood Hinton test was negative. The blood nonprotein nitrogen was 36 mg. per 100 cc., and a phenolsulfonephthalein test showed 5 per cent excretion in fifteen minutes, with 25 per cent excretion at the end of six hours (the patient had been unable to void at the proper time). The visual fields were normal except for bilateral enlargement of the blind spots. X-ray examination of the chest revealed a heart slightly enlarged in the region of the left ventricle. The aorta was markedly elongated and tortuous, with some generalized dilatation and slight calcification. The lung fields were clear.

The temperature, pulse and respirations remained normal for five days, and he was apparently getting along well. On the sixth day at 8 p.m. he complained of a sudden severe bilateral mid-back pain, which apparently radiated upward to the region of the neck and head. He perspired profusely. The pulse was strong and rapid, with a blood pressure of 242 systolic, 144 diastolic. He groaned, was disoriented and made statements that he would die that night. Paraldehyde and luminal were administered. He arose and, with assistance, "walked off" the pain in five minutes. There were no reflex changes. He complained of no pain for the remainder of the evening. The next morning he was stuporous, semicomatose and under the influence of paraldehyde. He did not respond to painful stimuli, but was able to move all his extremities. That afternoon he conversed with his wife, did not mention any pain and said he "felt fine." The temperature, pulse, respirations and blood pressure continued to rise as they had for the previous day. In the evening he became noisy and active, and then died. He continued to breathe three minutes after the heart had stopped beating.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: This man's illness had a very abrupt onset: there was not a slowly increasing amount of headache. Something apparently happened acutely.

I shall discuss this case in two parts, because the second half of the illness, although indirectly related, is not a part of the first. Headaches, disturbance of vision, vomiting (not extreme or per-

sistent), fainting spells and, on one occasion, a fall, when he was unconscious a few minutes, were the chief complaints. There was also loss of weight, with impairment of memory, dyspnea, orthopnea and nocturia. Such evidence of circulatory disturbance in the head with increased pressure might come from a variety of causes, including brain tumor, perhaps with hemorrhage into it to explain the sudden onset of symptoms. However, as we go on down the list of symptoms to the findings on examination we note hypertension, and we know that hypertensive encephalopathy can almost exactly mimic increased intracranial pressure due to tumor, especially when the hypertension enters the malignant phase. I do not believe that we can explain the situation wholly by the gradual development of increasing intracranial pressure. There may have been increasing pressure from edema, but the very beginning was sudden and that does suggest a definite vascular lesion, either a hemorrhage, an expanding small aneurysm or an infarct, or, as I said, there may have been a tumor with hemorrhage. It is not likely that an abscess could explain the situation with so long a story and without fever. Usually there are increased spinal-fluid pressure and superimposed cerebral edema with such small or large cerebrovascular lesions, and cerebral arteriosclerosis is always present in this group of cases. Hypertensive encephalopathy is more likely than is brain tumor. At the end of the first paragraph there is a little evidence of coronary and renal involvement, associated with the hypertension. The eyeground changes are characteristic of severe hypertensive retinopathy. Physical examination revealed no evidence of cardiac enlargement, but x-ray examination did show slight increase in the size of the left ventricle, as we should expect. It is quite likely that some hypertrophy of the heart was found, without much dilatation and with little or no evidence of failure, despite the history of dyspnea and orthopnea. Some renal vascular involvement was almost certainly discovered.

Certain intracranial tumors have been associated with hypertension, especially Cushing's syndrome (basophilic adenoma of the pituitary gland), but the other characteristics of Cushing's syndrome are not present, and we need not consider that further. The spinal-fluid findings I do not believe are diagnostic. Inflammatory changes, degenerative changes or tumor could each account for the increased protein; and exudation of serum around a small hemorrhage could account for some. We might have a comment on that point later by Dr. Kubik.

Apparently there was no uremia, although renal involvement was evident.

Thus I believe that a severe grade of hypertension, without any past history indicating a nephritis as a background, and without the certainty of any other complication, such as a tumor, was the explanation of the findings in the first part of the record.

The thing that killed him is, I think, related to the hypertension. It began with sudden severe transitory mid-back pain radiating upward, not downward as pain from the kidney would do. There is no statement about radiation to the front of the chest. We have just seen, at medical grand rounds, an unusual case of coronary thrombosis, with pain starting in the back but radiating to the front of the chest. In the present case the pain remained in the back; certainly that would be an unusual story for a coronary thrombosis that occurred as a fatal complication of hypertension.

Terminally the systolic pressure was considerably higher than it was at the previous reading; the diastolic pressure was about the same.

We have all become schooled here in the past few years to the idea that sudden severe pain in the back in hypertensive patients may be due to a dissecting aortic aneurysm, and that seems to be the probable diagnosis in the present case, even though the condition is rare, and even though this description fits it almost too well. Pulmonary embolism or another complication of that sort is not so likely. The episode that caused the pain in the back can be explained by final rupture of the aorta into the pleura, mediastinum or elsewhere. I think then that I shall follow what I believe is a conservative course, and diagnose this case as malignant hypertensive disease with some involvement of the heart and kidneys therefrom and with marked involvement of the brain, including a good deal of cerebral scarring and vascular disease and perhaps infarction or even a small aneurysm that has increased in size, not on a syphilitic basis, and aortic disease with dissection of the aortic wall, aneurysm and rupture.

Dr. Tracy B. Mallory: Assuming that the death was due to dissecting aneurysm, Dr. White, how would you explain the fact that he did not develop paralysis of the legs, which is usual?

Dr. White: One case I remember very well — the first one we analyzed correctly — was diagnosed despite the fact that we felt a good pulse in both feet; that finding, however, was one of the things that made us hesitate to make the diagnosis. There was a rupture of the dissected wall

into one of the iliac arteries, which had prevented the compression and occlusion of those vessels. Such might have occurred in this case.

DR. BERNARD M. JACOBSON: The diagnosis of the medical service up to the day of death was that given by Dr. White — hypertension with cerebral involvement. We saw him the morning after the episode of pain and were very much impressed by the fact that the patient was irrational and stuporous and somewhat under the influence of paraldehyde. The cerebral symptoms were so marked the evening before and the pain was so transitory that we believed he had been suffering from a cerebral vascular accident, probably hemorrhage. The lungs that morning were entirely filled with rales, and surprisingly enough, the pulse was very firm and the blood pressure higher than it had been the day before. My guess at that time was that he had a diffuse bronchopneumonia and the day before had had a cerebrovascular accident.

CLINICAL DIAGNOSES

Malignant hypertension with hypertensive encephalopathy.
Retinitis.
Nephrosclerosis.

DR. WHITE'S DIAGNOSES

Hypertensive cardiovascular disease (malignant phase).
Hypertensive encephalopathy with multiple vascular lesions.
Left ventricular cardiac hypertrophy.
Vascular nephritis.
Dissecting aneurysm of the aorta, with rupture into iliac artery or external rupture with fatal hemorrhage.

ANATOMICAL DIAGNOSES

Dissecting aneurysm of the aorta extending into the superior mesenteric, renal and common iliac arteries, with rupture into the pericardium.
Hemopericardium.
Cardiac hypertrophy, hypertensive type.
Pulmonary congestion with slight edema.
Arteriosclerosis of coronary arteries, aorta and cerebral arteries, minimal.
Infarction of pons.
Nephritis, chronic vascular.

PATHOLOGICAL DISCUSSION

DR. MALLORY: We found in this man an extensive dissection of the entire aorta. The rupture through the intima had occurred at the mouth of the innominate artery, and dissection had spread both upward as far as the annulus of the aortic valve and downward as far as the iliac arteries. Throughout the entire course of the aorta the wall was split into two complete layers separated by clotted and fluid blood. In the lower abdominal aorta, 7 cm. below the inferior mesenteric artery, a second intimal rupture had occurred, through which the current of blood was able to escape back into the original lumen; therefore there was no shutting off of the circulation in the legs. The dissection had extended a few millimeters to centimeters down a number of the small and large branches of the aorta. The mesenteric arteries and the renal arteries, for example, showed dissections 2 or 3 cm. in length. As in most cases of dissecting aneurysm the outer layer eventually gave way and hemorrhage occurred. In this case it was into the pericardium, and the presence there of 700 cc. of blood is enough to warrant the presumption that he died of cardiac tamponade. The other findings in this case, I think, are to be grouped together as those characteristic of hypertension. The heart was hypertrophied, particularly the left ventricle.

DR. WHITE: How much did it weigh?

DR. MALLORY: Five hundred grams. The kidneys were distinctly smaller than normal — 250 gm. — and showed the characteristic appearance of so-called "malignant vascular nephritis." The brain showed a few lesions which Dr. Kubik will describe.

DR. CHARLES S. KUBIK: It is curious that we find so little at autopsy to explain the cerebral symptoms in these hypertensive cases. In many of them, as Dr. White said, the spinal-fluid pressure is elevated, but in others with severe headaches the pressure may be normal. The total protein of the spinal fluid is often elevated up to 70 or 80 mg. per 100 cc., usually some figure less than 100 mg. I do not know of any other case in which the total protein has been over 200 mg., as it was here. A number of tiny hemorrhages were present in the pons, cerebral cortex and subcortical white matter. All of them were less than 1 mm. in diameter, some scarcely larger than a pinpoint. They varied in color, thus indicating that some were older than others. Sections showed so-called "ring hemorrhages" surrounding thrombosed arterioles and small arteries. One hemorrhage, a little larger than the rest, situated on the surface and involving the subarachnoid space, may possibly have been responsible for the first headache, which had a sudden onset and was particularly severe. There were also small infarcts in the pons and in the basal ganglia, the largest

one measuring less than 0.5 cm. in diameter. There are many things about these cases that I do not understand. In some of them where a high spinal-fluid pressure had been recorded during life we have not found any evidence of increased intracranial pressure at autopsy. The explanation may be a temporary circulatory disturbance which had subsided before death.

CASE 26342

Presentation of Case

A sixty-five-year-old widow was admitted in coma.

The patient was apparently well until six years before entry, when she began to note dyspnea on climbing stairs, and persistent ankle edema. She consulted her physician who diagnosed "leaky heart valves," but offered no treatment. Her complaints subsided somewhat following this episode, and she was fairly well until two years before admission, when jaundice and weakness appeared. She was told by another physician that she had a severe blood disease, and was then treated with injections three times a week for a "long time." Tiring of this the patient lapsed in her treatment, but as her symptoms returned, she again consulted her physician, who informed her that her disease had progressed far and that she would have to eat half a pound of raw liver every day. This regimen was too rigid for her, and she remained on it for only six months.

Several months before entry she developed nervousness, prominent eyes and a ravenous appetite, but in spite of the latter she lost 30 pounds in weight, dropping from 190 to 160 pounds. The patient became progressively weaker, and one week prior to hospitalization went to bed. She became so weak and clouded mentally that she failed to recognize her family. Although she had no pain, her physician had injected morphine about twenty-four hours before admission. Thirty minutes later she became unconscious, and remained in a stupor from which she could not be aroused.

The family, marital and past histories were noncontributory.

Physical examination revealed a well-developed, obese, moderately icteric woman in coma, whose breathing was slightly stertorous. The skin was dry, and the mucous membranes pale. There was a marked exophthalmos, with chemosis and icteric scleras. The retinal vessels were moderately sclerotic, with two small hemorrhages on the right. The disks were flat. The pupils reacted slightly to light. The thyroid gland was not remarkable. The lungs were clear throughout. A coarse systolic murmur was heard over the whole precordium; the rhythm of the heart was regular; the aortic second sound was greater than the pulmonic. The liver edge was palpated a handbreadth below the costal margin, and that of the spleen was noted two fingerbreadths below. There was slight non-pitting edema of the lower extremities. All the reflexes were normal, equal and active, except for the plantars which were equivocal.

The temperature was 99°F., the pulse 110, and the respirations 20.

Laboratory examination revealed a negative urine except for a ++ bile test. The blood showed a red-cell count of 1,420,000, with 36 per cent hemoglobin (Sahli), a hematocrit of 18 per cent, a color index of 1.2, a mean corpuscular volume of 126 cu. microns and a reticulocyte count of 6 per cent. There was a white-cell count of 21,000. A differential count showed 25 per cent polymorphonuclears, 5 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophils, 15 per cent myelocytes, 4 per cent megaloblasts, 16 per cent erythroblasts and 31 per cent normoblasts. The stools were guaiac negative. A blood Hinton test was negative. Lumbar puncture revealed normal dynamics, with a xanthochromic fluid and 400 and 280 red blood cells per cubic millimeter in the first and second tubes respectively; the ammonium sulfate ring test was positive. The blood nonprotein nitrogen was 66 mg. per 100 cc., and the chlorides were equivalent to 116 cc. N/10 sodium chloride. The carbon-dioxide combining power was 56.2 vol. per cent; a van den Bergh test was unsatisfactory.

The patient was given three 500-cc. transfusions, parenteral fluids with glucose, tube feedings, intramuscular liver and vitamin B_1. The temperature rose to 101°F. on the second and third hospital days; the pulse ranged around 90, and the respirations varied between 20 and 25. She became less active and developed rales throughout the right chest posteriorly. Respirations became labored, with dilatation of the nasal alae. Purulent sputum appeared in the throat, without expectoration. She rapidly failed and died on the second hospital day.

Differential Diagnosis

Dr. Alfred Kranes: As is the case with many patients admitted in coma, there are many gaps in the history which one would like to have filled in, but which friends and relatives of a patient frequently cannot supply. One would like to know, for example, whether the jaundice which

had been noted two years before admission had been constant or intermittent, whether it was associated with any changes in the color of the urine or stools and whether there had been any pain. It would also be of considerable value to know whether the injections, which presumably consisted of liver extract, had resulted in any improvement. The fact that she discontinued treatment might mean either that she had recovered sufficiently so that she felt it was no longer necessary or that she had become discouraged over the failure to improve. Because of the statement that she again consulted her physician when her symptoms returned, we might infer, however, that she actually did improve. It would also be of considerable help to know whether the half pound of raw liver a day for six months resulted in any improvement.

I do not quite know how to evaluate the nervous symptoms which developed prior to admission. The description sounds a good deal like the picture of thyrotoxicosis, but certainly that cannot be the whole story. If she did develop thyrotoxicosis, it must have been in addition to whatever preceded it. One would also like to know whether there were any paresthesias of the extremities.

So far as the physical examination goes, there is evidence of enlargement of both the liver and spleen, although I must add here that the liver being palpable a handbreadth below the costal margin does not necessarily mean it will be increased in size post mortem. All too frequently the clinical and pathological size of the liver do not agree, as has so often been pointed out in these exercises. The presence of marked exophthalmos seems to confirm the thyrotoxic symptoms as given in the history.

The laboratory tests are extremely helpful. The blood examination indicates the definite presence of a hyperchromic macrocytic anemia that was quite typical of pernicious anemia except for the white-cell count and smear. An elevated white-cell count is not usually seen with pernicious anemia, but it may occur in the presence of an acute infection; in this case the elevation may be more apparent than real because the count probably included an enumeration of the many nucleated red cells which were found.

So far as the lumbar puncture goes, one cannot be certain from the data here whether or not there had been a subarachnoid hemorrhage. The xanthochromic fluid may merely have been the result of prolonged jaundice and the red cells may have been traumatic, particularly since the number diminished in the second tube. I do not believe we can attach too much importance to the elevated nonprotein nitrogen since the blood sample was taken the day before death. There seems to have been no other indication of renal damage. The urine is stated to have been normal, although no specific gravity is mentioned.

As for the differential diagnosis, the patient apparently had a chronic disease which had been going on for six years with remissions and which probably responded, at least on one occasion, to parenteral liver injections. In addition the blood examination reveals the presence of a hyperchromic macrocytic anemia which was quite consistent with pernicious anemia. We have the additional information that it was megaloblastic. I do not see, therefore, how we can escape the diagnosis of pernicious anemia. The presence of jaundice and a severe anemia always raises the question in a patient of this age of an acquired hemolytic anemia, which would seem to be excluded by the large diameter of the red cells, by the absence of a marked reticulocytosis and by the finding of bile in the urine.

The diagnosis of pernicious anemia is of course consistent with the presence of chronic icterus, but there are certain features here which point in addition toward an intrinsic disease of the liver as the cause of the icterus. In the first place, the excretion of bile in the urine is very unusual in uncomplicated pernicious anemia. Nor is it usual to have the liver enlarged as much as appears to have been the case here. Another fact which points toward diffuse liver disease is the apparent remarkable sensitivity to morphine. You will remember that she went into coma shortly after an injection of morphine, from which she never recovered. There are two diseases in which this sensitivity occurs. One is myxedema, the other is diffuse liver damage, usually cirrhosis. There certainly is no evidence of myxedema in this case, and we do have evidence pointing toward liver disease. On the basis, therefore, of chronic jaundice, urobilinuria, enlarged liver and spleen and sensitivity to morphine, I am inclined to think that she did have a cirrhosis of the liver; just what type of cirrhosis I should not venture to guess.

The presence of a macrocytic anemia has frequently been described in association with liver disease, and I believe such is the case here. Many of these patients are resistant to liver therapy for some inexplicable reason. Of course, we do not know that this patient did not respond to liver since the history is very inadequate.

Whether or not she had thyrotoxicosis, I should not venture to state, since the evidence is too in-

conclusive. I think it would be foolhardy to make such a diagnosis in a patient who is admitted in coma and dies the next day. From the history and the exophthalmos, one might suspect its presence, but I do not believe we can go any farther than that. I shall, therefore, make diagnoses of cirrhosis of the liver of undetermined type, pernicious anemia and a terminal pulmonary infection, probably bronchopneumonia. There may also be some renal damage, which occasionally occurs in any jaundice of long standing — a so-called "bile nephrosis." We only have a single test of renal function taken the day before death — an elevated nonprotein nitrogen, which may mean nothing so far as anatomical damage to the kidney is concerned. We can go no farther than to mention this possibility.

Clinical Diagnoses

Pernicious anemia.
Bronchopneumonia.

Dr. Kranes's Diagnoses

Cirrhosis of the liver, type undetermined.
Pernicious anemia.
Terminal pulmonary infection (? bronchopneumonia).

Anatomical Diagnoses

Pernicious anemia, relapse.
Arteriosclerosis, generalized.
Extramedullary hematopoiesis, liver and spleen.
Nephritis, chronic, vascular, slight.
Jaundice, slight.
Ascites, slight.
Hydrothorax, slight, bilateral.
Leiomyoma, uterus.
Cholelithiasis.
Umbilical hernia.
Ovarian cyst.

Pathological Discussion

Dr. Tracy B. Mallory: The picture presented by this patient is one which some of the younger of us have perhaps never seen and which the older of us are in some danger of forgetting. Death primarily from pernicious anemia has become a rarity and can only result from the grossest medical incompetence or from a suicidal lack of cooperation on the part of the patient. The picture seen in this patient at autopsy was one which was very familiar prior to 1925 but is rarely seen in a laboratory of pathology at the present time. The entire bone marrow was hyperplastic, including that in the central portions of the long bones. On microscopic examination it was evident that the marrow was composed predominantly of erythroblastic elements, with a marked shift to the left and a predominance of megaloblasts. The next most numerous elements were large plasmatocytes containing many phagocyte red cells. Phagocytosis of red cells is, however, in all probability a postmortem phenomenon, as the late Dr. Francis W. Peabody showed in his classic studies of the marrow in this disease. Both the liver and spleen were moderately enlarged and showed considerable erythropoiesis, more than is usually found in a fatal case of pernicious anemia. The liver, in addition, showed extensive central necrosis, which is a usual finding. All the reticuloendothelial system showed some degree of hemosiderosis, much less, however, than is often seen. The heart was considerably hypertrophied and showed on microscopic examination many small scattered foci of fibrosis; there did not appear to be enough coronary narrowing to explain this. The thyroid gland was enlarged and nodular, but sections showed no evidence of hyperplasia. It is within the limits of possibility that she may have had true hyperthyroidism in the past which had undergone spontaneous remission, leaving, however, a permanent exophthalmos and a hypertrophy of the heart. This, however, is only speculation. There was no subarachnoid hemorrhage; in fact, we could find nothing beyond mild arteriosclerosis in the brain. The patient evidently had an idiosyncrasy to morphine, but I do not believe that on anatomical grounds we can incriminate either the thyroid gland or the liver as responsible for it.

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MEDICAL PREPAREDNESS: THE LISTING OF THOSE CONCERNED WITH MEDICAL CARE

THE second problem of medical preparedness has to do with the accurate listing of those who are qualified to participate in medical or public-health service. Such a list should include the names of physicians, dentists, public-health officers, nurses and laboratory technicians, and should be supplemented by specific information regarding age, marital status, experience, specialized training, teaching, hospital or other positions, and so forth. Only with the latter data on hand can intelligent choice of those best suited for the various types of service be made. Sufficient personnel must be left in all parts of the nation to provide adequate medical care for the civilian population; the staffs of medical, dental and nursing schools must not be so depleted that their teaching facilities are seriously impaired; and those who go into service must be assigned, so far as possible, to positions with responsibilities that, by training and experience, they are qualified to assume. During the rush that accompanied the mobilization of 4,000,000 men in 1917, these matters received scant attention, and the many mistakes that followed should and can be avoided.

The listing of the medical profession has already begun, the American Medical Association, through the Committee on Medical Preparedness, having forwarded questionnaires to every physician in the United States. When these have been filled out and returned all the data will be transferred to punch cards and, hence, be readily available. Furthermore, state and territorial chairmen on medical preparedness have been appointed, whose functions include contact with other state chairmen in their vicinities through the corps-area representative of the Committee on Medical Preparedness, the organization of state or territorial and county committees on medical preparedness, the promotion of civilian health, the dissemination of information to interested groups, the furnishing of additional data relative to the punch cards, the verification of the qualifications of physicians desired for service and the maintenance of adequate facilities for civilian medical care. In addition the Committee on Medical Defense adopted a resolution, a copy of which has been forwarded to various government officials in Washington, recommending that, in preparing for the conscription of personnel, provisions be made for the continuation of medical education and for the exemption of all medical students and interns in accredited and approved institutions.

All the necessary steps for the listing of physicians seem to have been taken. It remains for all physicians to fill out completely and correctly the questionnaire and to return it promptly, if they have not already done so. And it is to be hoped that information of a similar nature will be obtained from all groups, professional or otherwise, involved in medical and public-health services.

DRUGSTORE PRESCRIBING

Much activity in public health proceeds without penetrating the level of consciousness of practicing physicians. From time to time, they are made cognizant of this or that phase of public-health activity but often fail to maintain a continuing interest in this part of medicine. So long has the U. S. Public Health Service rendered important service to the country that its activities are apt to be taken for granted. This valuable governmental agency one is prone to associate with the old Hygienic Laboratory, now the National Institute of Health, and the various hospitals that it runs, and its co-operation with other agencies concerned with the health of the country are overlooked.

A recent activity of deep concern to all is the problem of venereal-disease quackery. The widespread campaign inaugurated against syphilis by Surgeon General Parran makes one forget the toll of gonorrhea. Indeed, it may not be too exaggerated to state that the greatest advance in many centuries in the treatment of gonorrhea — the use of sulfanilamide — may prove to increase rather than decrease half-treated cases produced by quack and "counter prescribing."

The trends in this direction are indicated clearly in the report* of a study conducted by the American Social Hygiene Association, in co-operation with the U. S. Public Health Service. A nation-wide survey of over a thousand drugstores in thirty-five cities, widely scattered, indicates the prevalence of drugstore prescribing and the sale of alleged remedies for self-diagnosed syphilis or gonorrhea. Approximately half the drugstores visited urged the patient to see a doctor but were willing to sell bottled remedies when asked for by name. Of thirty different preparations found to be generally available, only three or four contained substances recognized in the treatment of these diseases, the remainder being completely worthless mixtures. The cost of these "remedies" varied from one to three dollars a bottle for ingredients costing a few cents and worth nothing to the purchaser.

In comparison with a similar survey made in 1933, there is a statistically significant increase in "counter prescribing." Particularly pertinent is the fact that of the drugstores visited in 1933, about 30 per cent refused either to diagnose or to sell remedies without prescriptions; in 1939 only 7 per cent fell into this group. Advertising, on the whole, appears to have declined. In the 1933 survey it was pointed out that a total of nearly five million people believe themselves to have either gonorrhea or syphilis, whereas only two and a half million go to doctors for treatment.

The attack on this problem lies primarily in the suppression of the quack druggist, the continuing education of the ethical pharmacist through schools of pharmacy, pharmaceutical associations and trade and professional journals, and the eradication of the unethical medical practitioner. But the medical profession should help in the education of the laity, particularly in hospitals and clinics where poster advertising with slogans such as "Beware of Drugstore Prescribing!" might prove effective in spreading information among those classes most susceptible to this cruel type of charlatanism.

*Edwards, M. S., and Kinsie, P. M.: Illegal and unethical practices in the diagnosis and treatment of syphilis and gonorrhea. *Ven. Dis. Inform.* 21:1-10, 1940.

MEDICAL EPONYM

Courvoisier's Law

The following translated quotation is taken from *Casuistisch-statistische Beiträge zur Pathologie und Chirurgie der Gallenwege* [Critical and Statistical Contributions to the Pathology and Surgery of the Bile Ducts] (Leipzig: F. C. W. Vogel, 1890) by Professor Ludwig G. Courvoisier (1843–1918), of Basle, Switzerland:

> It is usually stated in reference books and textbooks that obstruction of the common bile duct leads to enlargement of the gall bladder by bile stasis. My experience is quite the opposite, and I am compelled to look on absence of distention in the presence of obstruction of the duct as characteristic of stone, and its presence as indicative of occlusion due to some other cause. If this observation should be further confirmed, we should have here an important fact on which to base a differential diagnosis.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

STATE COMMITTEES ON MEDICAL PREPAREDNESS

Each state committee on medical preparedness, according to the plans advocated by the Committee on Medical Preparedness of the American Medical Association, is to consist of the president and secretary of the state medical society, the appointed chairman of the committee and the member or members of the Committee on Medical Preparedness within whose corps area the state is located and such other members as this group may select.

For Massachusetts this includes Dr. Walter G. Phippen, both as president and as First Corps Area representative of the Committee on Medical Preparedness, Dr. Alexander S. Begg, both as secretary and as appointed chairman, and Dr. Stanley H. Osborn, of Hartford, Connecticut, as the second First Corps Area representative of the Committee on Medical Preparedness.

The other state chairmen for New England are as follows:

CONNECTICUT: Dr. George M. Smith, Pine Orchard
MAINE: Dr. John G. Towne, Waterville
NEW HAMPSHIRE: Dr. Deering G. Smith, Nashua
RHODE ISLAND: Dr. Halsey De Wolf, Providence
VERMONT: Dr. Benjamin F. Cook, Rutland

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

PREGNANCY AND LABOR COMPLICATED BY PNEUMONIA

Mrs. C. H., a twenty-nine-year-old para II, was admitted to the hospital at 1:15 a.m. on March 6, 1939. She was not in labor, but complained of a headache, a cough and pains in the chest and shoulder. She stated she had had a severe chill lasting ten minutes just before being admitted to the hospital.

The family and past histories were not important. At the time of the previous delivery the patient was admitted with an upper-respiratory condition which was moderately severe; the temperature rose to 101°F. and the pulse to 120.

The temperature on admission was 101.8°F., the pulse 120, and the respiration 25. Four hours later the temperature had risen to 103.8°F., the pulse to 140, and the respiration to 30. A medical consultant was called, and the opinion was given that the patient had a definite early pneumonia. Physical findings showed dullness and impaired breath sounds over the left base and patches of consolidation on the right side. The white-cell count was 46,100. Cultures from the throat were taken. A chest plate was ordered. The x-ray report read, "There is mottled density at both bases; the upper lung fields are clear." An initial dose of 30 gr. of sulfapyridine was given, and this was repeated in four hours; thereafter 15-gr. doses were given at four-hour intervals.

The culture showed a Type 7 pneumococcus. In view of this finding, 100,000 units of Type 7 antipneumococcus serum was ordered. Skin and eye tests were negative; 20,000 units of serum was given at 7:30 p.m., and since no reaction followed, the remaining 80,000 units was given at 9:30 p.m. Mild labor began about the time of the first injection of serum; the pains were of moderate intensity, and to ensure as much rest as possible ⅓ gr. of Pantopon was given at intervals during labor. Labor continued uneventfully, with cough and general discomfort helped by Pantopon, until 5:30 a.m., when the cervix was fully dilated and the membranes bulging. The membranes were immediately ruptured, and the head came down on the perineum. Under 1 per cent novocain infiltration, a small median episiotomy was made, and a male child, weighing 8 pounds, 8 ounces, was delivered. The baby cried spontaneously. The placenta and membranes were delivered intact, and the episiotomy wound was repaired with No. 0 chromic catgut.

The immediate condition after delivery was fairly good, with a pulse of 124 and a blood pressure of 100 systolic, 72 diastolic. At 8 a.m., three and a half hours after delivery, the temperature had dropped to 97.2°F., the pulse to 88, and the respirations to 14. Sulfapyridine was omitted at this time, since the patient complained of nausea and itching over the upper chest. Codeine was given to control cough, and no other medication was ordered.

On the third postpartum day there was a good deal of pain on the left side, with diaphragmatic spasm. Patchy bronchial breathing could be heard, but in view of the normal chart it was believed that these areas would resolve. On the sixth postpartum day definite fluid on the left was noted, but no indication for paracentesis was found. X-ray examination confirmed the physical findings. The white-cell count at the time was 11,000, with the temperature about 99.5°F. Twelve days post partum fluid could still be demonstrated but the temperature was normal and the patient felt well. Improvement continued in the subsequent week,

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

and the patient was discharged home well on the twenty-second postpartum day, with a healthy baby doing well on a formula.

Comment. The happy result in this case was undoubtedly due to the promptness of diagnosis and of treatment. Within twenty-four hours after the initial chill the temperature was dropping; thirty-two hours after admission it was normal, and except for a slight rise from the fifth through the ninth day, due to fluid, remained there. Pantopon, in ⅓-gr. doses, gave the patient much comfort and aided in maintaining the best possible condition. Novocain infiltration worked extremely well, the episiotomy being repaired without incident. It seems quite remarkable that a patient can go through a definite pneumonia, be delivered and again have a normal temperature all within thirty-six hours.

COMMITTEE ON INDUSTRIAL HEALTH

The following cases represent situations which could arise at any time in industry. They are noteworthy in that they are preventable, yet they could occur and did occur in industries endeavoring to take all adequate steps in matters pertaining to the safety and health of employees.

Metal Fume Fever

A forty-seven-year-old Irish-American, who had been employed as a molder in a brass foundry for about twenty years, was seen by the company physician as the result of a telephone call from the man's wife. She stated that for some months previously her husband had come home every Monday night with a headache, which during the course of the evening developed into a severe shaking chill. The latter lasted approximately half an hour and was followed by a fever, with very profuse sweating. By the next morning he was entirely normal, and remained so until the following Monday evening. The patient was questioned in regard to these symptoms and freely admitted them. He stated that he had this difficulty only in the winter, when closing the windows in the foundry decreased the natural ventilation. The situation had never bothered him so much as it did his wife, and he had not mentioned the matter to any physician, possibly because of some fear that he might lose his job.

In the course of this man's work he was required to pour molten brass into molds, this operation lasting about ten minutes and being repeated four or five times a day. The alloy in question contained 5 per cent zinc. While pouring the molten metal he frequently had a small cloud of white fumes blowing directly into his face; analysis of these fumes confirmed the presence of a considerable amount of zinc.

Further recurrence of this man's difficulty was entirely prevented by having him wear an approved respirator during the periods when he was engaged in pouring molten metal.

Comment. This case is quoted as a typical story of metal fume fever, known also as "brass chills" and "brass founders' ague." Characteristically, one attack confers immunity on the individual so long as he continues repeated exposures to the fumes. This immunity is lost over a week end, holiday or vacation, and the individual becomes susceptible to another attack. Prevention of this condition consists of adequate ventilation, or protection from the fumes by means of an approved respirator.

Fume Intoxication

A twenty-eight-year-old American was employed painting the inside of a large steel casing. This was roughly in the shape of a huge bath tub, completely open at the top, and approximately 12 ft. long, 4 ft. wide and 5 ft. deep. He was applying with a brush a varnish in which the solvent was composed of equal parts of toluol and high-flash naphtha. Working on the inside of this casing he naturally enough started painting at the top, gradually working toward the bottom. After some little time he found that he was becoming extremely dizzy and was unable to climb out; with considerable difficulty he attracted the attention of a nearby workman and was lifted out in a semiconscious condition. He was unable to walk unassisted and later stated that he had a "pins-and-needles feeling all over his body." He struck one of the men who was assisting him, although he did not remember what produced this outburst of temper. He was taken immediately to the plant dispensary, where he was found to be markedly cyanotic, with a respiratory rate of 10 and a pulse rate of 50. The skin was cold and clammy, and he was still only semiconscious. Oxygen and carbon dioxide were administered by means of an H & H inhalator, and complete recovery was very rapid. Less than an hour later he was taken home feeling perfectly well.

Comment. This case undoubtedly represents acute intoxication by the fumes of a mixture of toluol and high-flash naphtha. It is here presented as a reminder that danger can easily be present even though a man is working in a location which would not ordinarily be regarded as an enclosed place. Here the entire top of the casing was wide open, but the fumes of the solvent, being heavier than air, completely filled the lower portion of the casing in such concentration as to create an extremely hazardous condition. This case could easily have had a fatal outcome. The most satisfactory form of prevention in a situation of this sort consists either of adequate ventilation of the inside of the casing or of providing the employee with an air-lined respirator. Precautions of this sort would automatically be employed if a man were being sent inside a closed tank. Care must be taken to see that similar conditions do not arise even though the area in question is not completely enclosed.

Tooth Etching

A battery repairman of one year's service reported at the clinic that he had been advised by his dentist that the enamel of his incisor teeth was being destroyed by the fumes present in the battery room.

Examination revealed that all buccal surfaces of the incisors not in contact with the lips during ordinary conversation presented an etched or ground-glass appearance. In fact, the cutting edge of these exposed teeth had been so eroded that the dentine was exposed and had become darkened. Examination of this man's saliva revealed a pH of 6.1. A fellow employee with etched teeth showed a pH of 5.4 in the saliva.

About 20 per cent of the employees in the repair division were found to exhibit more or less etching of the incisor teeth.

Although these cases were not considered as industrial accidents by the insurance carrier, an industrial accident

board awarded lump-sum payments for the porcelain jacketing of affected teeth.

Comment. A battery repair gang spends 30 to 40 per cent of a day in an atmosphere filled with droplets of sulfuric acid. This concentration of acid causes a choking and coughing for a few minutes in persons not accustomed to it.

Those men whose tooth enamel is affected by sulfuric acid seem to be either habitual mouth breathers or those with deficient or soft enamel structures. The habitual mouth breathers are affected because the acid deposited on the exposed teeth is not immediately diluted with saliva and thus tends to etch the enamel.

Personal communications with New England battery manufacturers and the Submarine Service of the U. S. Navy failed to reveal a similar situation with them. However, in the Middle West, industrial physicians have long been familiar with this condition.

Wearing of a filter mask, habitual nose breathing and the chewing of Oralgene Gum (containing magnesium oxide) have checked the incidence of tooth etching.

DEATH

RENAUD — ULRIC J. RENAUD, M.D., of Brockton, died August 12. He was in his forty-fourth year.

Dr. Renaud received his degree from Bowdoin Medical School in 1919 and served his internship at Central Hospital, Lewiston, Maine. He was a member of the Massachusetts Medical Society and the American Medical Association.

Two daughters, his mother and father and a sister survive him.

CORRESPONDENCE

REGIONAL FRACTURE COMMITTEES

To the Editor: The following remarks were delivered by me, as chairman, at the annual meeting of the regional fracture committees of the American College of Surgeons for each of the New England states. I believe that they may be of interest to your readers.

CHARLES L. SCUDDER, M.D.
374 Commonwealth Avenue,
Boston.

* * *

There are in the United States and Canada today about eighty regional fracture committees. Obviously, certain states and provinces have more than one committee. The aim of the General Fracture Committee, of which we here are a part, is to improve the treatment of fractures. You in this audience represent many communities throughout New England.

It is a generally recognized fact that surgeons have in times past been much more interested in pathological surgery than in purely traumatic surgery. Thus, the attention of surgeons and of general practitioners of medicine has not been focused on the recognition, treatment and end results of fractures. However, for over fifteen years, there has been developing in this country an increasing interest in fractures. With the rise in the incidence of fractures, with the increase in the complications attending fractures and with the occurrence of fractures and multiple injuries in rural districts, there has developed a definite demand for the services of medical men in caring for fractures.

It appears that many medical men are not only uninterested but unskilled and untrained in the treatment of these injuries. Moreover, many of these practitioners do not know that they are unable, or if they know, do not admit it; and unbelievably poor functional results follow improper treatment. The causes of such lamentable unpreparedness on the part of the general practitioner are that in the medical school he had little or no instruction in the treatment of fractures and that since graduation he has not studied to perfect his treatment of these cases.

In order to improve the treatment of this increasingly important group of cases, there are three points of attack for us as members of the regional fracture committees: the undergraduate student; the practitioner of medicine; and the lay public.

There is at present a movement on the part of our educational committee to improve fracture instruction given in undergraduate medical schools in this country. Each of the seventy-eight medical schools is being approached by members of regional committees. Because of recent developments in the training of interns, residents and surgeons, it is becoming more and more evident that the medical school will never be able to deliver to the community a practitioner fitted to take care of fractures. Consequently, it is a part of our function as regional-committee members to insist that certain fundamentals be taught the medical student, and to help the practitioner to do those things in a fracture case which he can learn to do.

It is the aim of the members of the regional committees not only to perfect their own treatment of individual fractures but to see to it that every doctor in each rural community is taught to recognize a fracture when he meets it; to know when he cannot treat it; to understand how to transport safely such a victim of fracture to the nearest hospital where x-rays are available and films can be interpreted; and further, to realize the importance of immediately bringing the victim and a trained surgeon together.

The fact that here among ourselves exist differences of treatment of individual cases is reason enough for stressing first-aid and transport to a hospital where proper care can be given. The conditions in apparently similar fractures are so different that the treatment of fractures never should be standardized. However, first aid and transport may be and are standardized.

Difficulties in the making of a living for one's family and dependents are today more and more in evidence. Doctors are turning with avidity to traumatic surgery, but the vast majority of these men are without training or experience for such work. The public suffers; it is conscious of this mediocre treatment and rightly demands something better.

Through properly edited propaganda, lay people may come to learn that early recognition, painless transport, careful x-ray study and skilled treatment may be properly demanded by a person with a fracture. These same lay people may be instructed not to ask the surgeon for impossibilities. Because Neighbor Jones, following a fracture of the leg, walked a certain number of weeks afterward, is no reason why someone else with a broken leg should expect to walk as soon as he did. Professional criticism and impossible demands of ignorant laymen lead to suits for malpractice.

I am proud of the development of the regional fracture committees of New England. This joint assembly of the committees of these closely affiliated states offers a very helpful opportunity to improve our points of view.

We have listened to splendidly presented papers on special subjects; we have still others to hear this afternoon. It is appropriate that we should accommodate ourselves to recent advances in fracture treatment; but let us not forget that, as a member of a state committee, each committeeman has a definite duty to perform toward the medical school, toward the general practitioner and toward the public.

The approved modern hospital is the workshop of scien-

tific medicine and surgery. All of you are attached to such hospitals, and it is through these hospital workshops that our best results may be expected. I cannot hope to tell you how to deal with your own special problems. That is the business of the state chairman to work out in conference with his secretary and others. Let each state committee help the practitioner, in the presence of a fracture, to avoid additional trauma and to hasten, by proper transport, the contact of patient and trained surgeon.

If I were asked to name a great improvement in fracture treatment, I should reply, the recognition of the importance of first-aid and transport, that is, the preparation of the patient for proper surgery.

NOTICES

SUFFOLK CENSORS' MEETING

The censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, Boston, on Thursday, November 7, at 4:00 p.m.

Candidates should make personal application to the secretary and present their medical diplomas at least six weeks before examination (if graduates of foreign medical schools or schools not on the list recognized by the Council, at least eight weeks before).

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Orthopedic Consultant
Salem	September 3	Harold C. Bean
Haverhill	September 4	William T. Green
Lowell	September 6	Albert H. Brewster
Gardner	September 10	Mark H. Rogers
Brockton	September 12	George W. Van Gorder
Pittsfield	September 16	Francis A. Slowick
Northampton	September 18	Garry deN. Hough, Jr.
Worcester	September 20	John W. O'Meara
Fall River	September 23	Eugene A. McCarthy
Hyannis	September 24	Paul L. Norton

MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

School Physician, $550 a Year, Revere

Director of State Civil Service, Ulysses J. Lupien, has recently announced that a competitive examination is to be held on September 28 in order to find eligibles for appointment to the position of school physician, School Department, Revere.

The entrance requirements are as follows: applicants must be registered physicians under the State Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2; practical questions, 3; total, 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is Saturday, September 14, at 12 o'clock noon.

CLINICAL CONGRESS OF THE CONNECTICUT STATE MEDICAL SOCIETY

The Clinical Congress of the Connecticut State Medical Society will be held at the Sterling Law Buildings, New Haven, on September 17, 18 and 19. Morning and afternoon sessions, beginning at 9:30 a.m. and 2:30 p.m. respectively, will take place on the three days. Papers will be presented by well-known specialists in their fields.

The special subjects for the three-day afternoon courses will be hematology, fracture treatment and recent advances in the therapeutics of gastrointestinal disease.

Full information may be obtained by writing to the Connecticut Clinical Congress, 258 Church Street, New Haven, Connecticut.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGY

There will be a meeting of the New England Society of Anesthesiology at the Boston City Hospital on Monday, September 16, at 8:00 p.m. Dr. P. D. Woodbridge will speak on the subject "Cyclopropane: Recent advances in precautions and usage."

1940 GRADUATE FORTNIGHT

The 1940 Graduate Fortnight of the New York Academy of Medicine will be held from October 14 to 25. The purpose of this meeting is to make a complete study and authoritative presentation of a subject of outstanding importance in the practice of medicine and surgery. The current topic is "Infections."

There will be a carefully integrated program, which will include morning panel discussions, afternoon clinics and clinical demonstrations at many of the hospitals of New York City, evening addresses and appropriate exhibits. The evening sessions at the Academy will be addressed by recognized authorities in their special fields, drawn from leading medical centers of the United States. The comprehensive exhibit will include books and roentgenograms, pathologic and research material, and clinical and laboratory diagnostic and therapeutic methods. It is also planned to provide demonstrations of exhibits.

The following subjects will be included: experimental basis of chemotherapy in the treatment of bacterial infections; clinical bacterial chemotherapy, results obtained and dangers encountered; a general consideration of bacterial infections; recent advances in knowledge of streptococcal infections; infections of the mouth, pharynx and upper respiratory tract; infections of the middle ear and nasal sinuses; infections of the teeth and surrounding structures; influenza; pneumococcal infections; bacterial meningitis; infections of the urinary tract; gonococcal infections in the male; gonococcal infections in the female; osteomyelitis and pyogenic infections of the joints; wound infections; puerperal infections; treatment of infections by methods other than chemotherapy; virus infections; acute poliomyelitis; brucellosis — undulant fever; rickettsial diseases; lymphogranuloma venereum; epidemic encephalitis; other forms of encephalitis and choriomeningitis; and exanthematous diseases.

The Academy provides this program for the fundamental purpose of medical education, consequently all members of the medical profession are eligible for registration. A complete program and registration blank may be secured by addressing: Dr. Mahlon Ashford, New York Academy of Medicine, 2 East 103d Street, New York City.

SOCIETY MEETINGS AND CONFERENCES

September 2–6 — American Congress of Physical Therapy. Page 862, issue of May 16.

September 12–May 8 — Pentucket Association of Physicians. Page 263, issue of August 15.

September 16 — New England Society of Anesthesiology. Notice above.

September 16–20 — American Occupational Therapy Association. Page 263, issue of August 15.

SEPTEMBER 17–19 — Clinical Congress of the Connecticut State Medical Society. Page 305.

OCTOBER 6–11 — Annual meeting of the American Academy of Ophthalmology and Otolaryngology. Page 81, issue of July 11.

OCTOBER 8–11 — American Public Health Association. Page 655, issue of April 11.

OCTOBER 11, 12 — Pan-American Congress of Ophthalmology. Page 898, issue of May 23.

OCTOBER 14–25 — 1940 Graduate Fortnight of the New York Academy of Medicine. Page 305.

OCTOBER 21 — American Board of Internal Medicine. Page 369, issue of February 29.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 1064, issue of June 20.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21–25 — American College of Physicians. Page 1065, issue of June 20.

DISTRICT MEDICAL SOCIETY

SUFFOLK

NOVEMBER 7 — Censors' meeting. Page 305.

BOOK REVIEWS

Hereditary and Environmental Factors in the Causation of Manic-Depressive Psychoses and Dementia Praecox. By Horatio M. Pollock, Benjamin Malzberg and Raymond G. Fuller. 8°, cloth, 473 pp., with 87 tables. Utica: State Hospitals Press, 1939. $2.50.

This book represents a very painstaking effort to assess through the statistical approach the relative importance of hereditary and environmental factors in the causation of manic-depressive psychoses and dementia praecox. In a general way it is well demonstrated that the incidence of socially inadequate persons as judged by specified criteria is greater in the families of large groups admitted to the Utica State Hospital for the first time because of their disease, than is that of social inadequacy in New York State as a whole. When the calculations are limited to the siblings of the patients, allowance being made for the living siblings who may yet become socially inadequate, an incidence of inadequacy much greater than the rate for the population as a whole is found. Siblings of female patients with manic-depressive psychoses show the highest incidence. The incidences of both manic-depressive psychoses and dementia praecox among the relatives and especially among the siblings of the patients with such ailments were considerably above that expected for the population of New York State as a whole. Although it seems clear enough that there is a heaping of cases of mental disease in the families of the patients, the incidence of cases in any family group is not large enough to fit any of the recognized mendelian ratios.

The statistical studies of environmental factors in the production of mental disease are very difficult to evaluate, since there are no control statistics. Furthermore, many environmental factors are not suitable for statistical study. For instance, such a simple factor as whether patients liked or disliked one or both parents is not capable of statistical treatment. In general this study shows a preponderance of environmental factors such as one would expect in the homes of people with "shut-in" personalities, for instance, parents who avoided social contacts. Severe mental stresses resulting from financial difficulties, worries over sickness or death in the family, sexual difficulties or severe disappointments had been frequently imposed on the patients just prior to the mental breakdown. If these immediately precipitating factors are of importance there is no difference in their character or incidence in the manic-depressive group, as compared with that in the dementia-praecox group.

Many case histories illustrating the occurrence of mental disease in the presence or absence of discernible hereditary or environmental factors are included in the volume, leading to the conclusions that there are probably all degrees of predisposition to these diseases and that the interplay of environment on predisposition probably determines the appearance or absence of overt mental disease.

Orthopedic Operations. By Arthur Steindler, M.D. 8°, cloth, 166 pp., with 322 illustrations. Springfield, Illinois: Charles C Thomas, 1940. $9.00.

In the present volume, Dr. Steindler has compiled a text which will be acknowledged as an outstanding reference book in the field of orthopedic surgery. Its material is so much more complete than that in the earlier editions that it amounts to an entirely new work on the subject, but his four cardinal principles have been retained and are worth a word of comment. As the author observes, he has approached his subject from the point of view of evaluating operative procedures: first, by the mechanical and physiological rationale of surgery; second, by corroborative experimental studies; third, by the comparison of operative technic with empirical experience; and last, by statistical end-result studies to justify operation. It is probably safe to say that no other surgical specialty involves such a wide choice of procedures or such debatable indications as orthopedics, and that, in consequence, a careful preoperative analysis along the lines suggested by these principles is invaluable.

In the first part of this work, general biological and clinical considerations are discussed somewhat briefly. The second portion deals with the technic of orthopedic surgery, as related to the various tissues, such as tendons, fascia, skin, nerves, joints and bones. The third section applies to specific orthopedic conditions and the indications for and the end results of operative treatment. These topics are presented in detail, and each chapter is accompanied by a complete list of references, making the volume almost a compendium of orthopedic literature. There are many carefully selected illustrations, which are most effective in emphasizing technical and anatomical principles.

Such a brief sketch of the material of this text gives an inadequate picture of its value. It represents an enormous amount of clinical experience with tested end results. To this has been added most painstaking study, so that methods favored by other authorities are presented with equal clarity as those of the author, and no important aspect of the discussion is omitted. For its comprehensiveness as well as its detail, this book deserves the highest recommendation.

Massage and Remedial Exercises in Medical and Surgical Conditions. By Noël M. Tidy, T.M.M.G. Fourth edition. 8°, cloth, 458 pp., with 182 illustrations. Baltimore: Williams & Wilkins Company, 1939. $5.25.

The third edition was reviewed in the September 20, 1938, issue of the *Journal*. The present edition differs very little from its predecessor. To quote from the preface: "The only new sections are short ones on myositis ossificans in Chapter II, and on the effects of gas poisoning in Chapter XXII. . . . The rest of the additions consist mainly of notes on such forms of electrotherapy as diathermy, short-wave treatment and ultra-violet ray or infra-red radiations."

The two new sections occupy a little over a page each. They present in condensed form the pathology, symptoms, complications and treatment of these conditions.

On the whole this book is meritorious.